Effects of light interventions for adaptation to night work

Simulated night work experiments

Erlend Sunde

Thesis for the degree of Philosophiae Doctor (PhD)
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Scientific environment

This doctoral thesis is based on studies conducted at the Faculty of Psychology, University of Bergen. The candidate was a Research Fellow at the Department of Psychosocial Science, Faculty of Psychology, University of Bergen, which provided fellowship, main supervision, and the PhD program. The candidate was enrolled at the Graduate School of Clinical and Developmental Psychology and was a member of the Bergen Sleep and Chronobiological Network.

The project included close collaboration with members of the Bergen Stress and Sleep Group at the Department of Biological and Medical Psychology, Faculty of Psychology, University of Bergen, that provided a scientific environment, and important contribution in the study design and data collection. Also important for this thesis was the scientific environment provided by the Department of Clinical Psychology, Faculty of Psychology, University of Bergen. The project also included collaboration with the Norwegian Competence Center for Sleep Disorders, Haukeland University Hospital.

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Abstract

In modern society, the need for 24-hr operation and services requires some people to work outside normal daytime work hours (i.e. shift work), including the night. For instance, healthcare, police, and transportation, are sectors where night work is common. Exposure to shift work, and particularly night work, can have negative impact on the workers' health. Especially, sleep is reported to be disturbed among night workers, as they must be awake at times they would normally be sleeping, and sleep at times they would normally be awake. This circadian misalignment of the sleep-wake rhythm may in a long-term perspective lead to ill health and diseases. Also, in a short-term perspective night work may cause adverse effects. Night workers experience increased sleepiness and performance deterioration during night shifts, and especially in the early morning hours, the sleep propensity and performance decrements are high. As such, night work has also been associated with increased risk of accidents and injuries.

Several countermeasures to reduce the adverse impact of night work have been suggested. Common strategies involve scheduled naps and caffein use. However, there is increasing interest in the use of light interventions for eliciting beneficial effects for night workers. Light exposure has the potential to entrain the biological circadian rhythm in humans, and as such can be used to produce circadian adaptation to a night work schedule. In addition, light has acute alerting effects which can reduce alertness deficits and improve performance during the night shift. Such effects rely on several characteristics of the light, such as timing, intensity, and wavelengths (spectral distribution). With the development of light emitting diode (LED) technology, new strategies for illumination of workplaces have emerged.

This thesis is based on three papers using standard ceiling mounted LED-luminaires to administer different light conditions during simulated night shift experiments. The main aim has been to investigate and elucidate how such LED lighting strategies can be used to facilitate adaptation to night work on measures of sleepiness, performance, and circadian rhythm.

In paper 1, the objective was to investigate how a full-spectrum (4000 K) bright light (~ 900 lx), compared to a standard light (~ 90 lx), affected alertness and performance during three consecutive simulated night shifts (23:00–07:00 hrs), as well as circadian phase shift after the simulated night shifts. Results indicated that bright light effectively reduces sleepiness, and improves performance during three consecutive night shifts, compared to standard light. Bright light seems to be beneficial in the later parts of the shifts, when sleep propensity is particularly high. For instance, in the later parts of night 2 and 3 it was found that the number of lapses of attention on a vigilance task revealed half as many lapses with bright light, compared to standard light. Furthermore, bright light induced a larger phase delay as compared with standard light, although data were incomplete, hence validation of these findings are needed.

The objective in the second paper was to investigate how short-wavelength monochromatic blue light (λ_{max} = 455 nm), compared to red light (λ_{max} = 625 nm) with similar photon density (~ 2.8 x 10^{14} photons/cm^2/s), affected alertness and task performance during one simulated night shift (23:00–06:45 hrs), as well as circadian phase shift following the night shift. The results in paper 2 suggest that monochromatic blue light reduces sleepiness and improves performance in the later parts of the night shift. Similar to the findings in paper 1, the number of attentional lapses with blue light was half of that seen with red light. Blue light also led to a larger phase delay of the circadian rhythm. There were indications of improved visual comfort with blue light, although both light conditions overall produced visual discomfort.

In the third paper the main aims were to investigate how polychromatic blue-enriched white light (7000 K; ~ 200 lx), compared to warm white light (2500 K) of similar photon density (~ 1.6 x 10^{14} photons/cm^2/s), affected alertness and performance during three consecutive simulated night shifts (23:00–06:45 hrs), as well as circadian adaptation to the night work schedule. The results indicated minor, yet beneficial effects of 7000 K light compared to 2500 K light, mainly in terms of fewer performance errors on a vigilance task in the end of night 1 and 2. No significant

difference in terms of circadian phase shifts were found between these two light conditions.

In conclusion, the papers suggest that standard ceiling mounted LED-luminaires have the potential to produce light conditions that may facilitate adaptation to night work. Paper 1 suggests that bright light improves performance and reduces sleepiness during three consecutive simulated night shifts. Results from paper 2 indicate that short-wavelength blue light improves performance, reduces sleepiness, and causes a larger phase delay than long-wavelength red light during one simulated night shift. Paper 3 indicates that using polychromatic blue-enriched white light has minor, yet beneficial effects on performance measures, compared to warm white light during three consecutive simulated night shifts. Further research is needed to validate and support the findings and investigate the impact and feasibility of similar light conditions in real-life workplaces. Future research should also explore more light conditions that can be favourable for night workers, in order to develop recommendations for illumination of night workers workplaces. Moreover, there is a need to elucidate potential long-term adverse health impacts of exposure to LED lighting.

List of Publications

Paper 1

Sunde, E., Mrdalj, J., Pedersen, T., Thun, E., Bjorvatn, B., Grønli, J., Harris, A., Waage, S. & Pallesen, S. (2020). Role of nocturnal light intensity on adaptation to three consecutive night shifts: a counterbalanced crossover study. *Occup Environ Med, 77*(4), 249-255. doi:10.1136/oemed-2019-106049

Paper 2

Sunde, E., Pedersen, T., Mrdalj, J., Thun, E., Grønli, J., Harris, A., Bjorvatn, B., Waage, S., Skene, D. J., & Pallesen, S. (2020). Alerting and circadian effects of short-wavelength vs. long-wavelength narrow-bandwidth light during a simulated night shift. *Clocks Sleep, 2*(4), 502-522. doi:10.3390/clockssleep2040037

Paper 3

Sunde, E., Pedersen, T., Mrdalj, J., Thun, E., Grønli, J., Harris, A., Bjorvatn, B., Waage, S., Skene, D. J., & Pallesen, S. (2020). Blue-enriched white light improves performance but not subjective alertness and circadian adaptation during three consecutive simulated night shifts. *Front Psychol, 11*, 2172. doi:10.3389/fpsyg.2020.02172

List of abbreviations

CBT	core body temperature
DLMO	dim light melatonin onset
DSST	Digit Symbol Substitution Test
EEG	electroencephalogram
GLMM	generalized linear mixed model
ipRGC	intrinsically photosensitive retinal ganglion cell
KSS	Karolinska Sleepiness Scale
λ_{max}	peak wavelength
LED	light emitting diode
LMM	linear mixed model
MEQ	Morningness-Eveningness Questionnaire
NOK	Norwegian krone
NREM	non-rapid eye movement
PANAS	Positive And Negative Affect Schedule
PER	period circadian regulator
PRC	phase response curve
PSG	polysomnography
PVT	Psychomotor Vigilance Task
REM	rapid eye movement
RT	response time
SCN	suprachiasmatic nuclei
SD	sleep deprivation
SD	standard deviation
SE	standard error

Contents

1. Introduction

Modern society has been termed ‘the 24-hr society’ due to increasing demands for continuous operation and services 24/7 [1]. Some services (e.g. emergency and healthcare, police, military, transportation, and some types of industry) obviously need to be available 24 hrs a day. Still, commercial interests have favoured 24-hr operation also in other sectors. Consequently, large parts of the work force are engaged in some form of shift work (i.e. irregular/unusual work hours) to sustain these demands. Among European workers, it has been reported that 19% are engaged in work during the night (≥ 2 hrs between 22:00 and 05:00 hrs) at least once a month [2]. As most adults spend a great amount of time at work, the workplace impacts the life of workers in various ways. Many values their job not merely as a means for making money, but also as an arena for personal development and social interaction. Furthermore, while there are many positive effects of work, the workplace can also be the origin for adverse health effects.

Working time arrangements has emerged as an important factor that can adversely impact workers health [3]. Shift work, and particularly schedules including night work, have been associated with increased risk for chronic diseases and adverse health effects [4]. Night work implies that workers must be awake at times they would normally be sleeping, and sleep at times they would normally be awake. Thus, a main challenge with night work relates to circadian misalignment of the sleep-wake rhythm, with night workers usually being partially out of phase with the biological circadian rhythm promoting wakefulness during the day and sleep during the night [5]. As such, night workers experience increased sleepiness and performance deterioration during night shifts [6]. These alertness and performance deficits have been related to the increased risk of injuries and accidents during night work [7].

Several measures to counteract the negative effects of night work have been suggested, e.g. forward shift rotation, naps, breaks, use of stimulants (caffeine), and bright light therapy [8]. However, there is still a need for investigating interventions that may effectively be implemented at real-life workplaces.

The potential beneficial effects of light exposure in terms of improved alertness and circadian adaptation have been known for many years [9, 10]. With development of light emitting diode (LED) technology, increasing interest in using light as a countermeasure has emerged. Cost-effective LED-based light sources can now be programmed to provide a range of different light conditions, both in terms of intensities and wavelengths, and LED-luminaires are now feasible as standard room lighting [11]. However, few studies have investigated such standard LED-based lighting during night work. Against this backdrop, the main purpose of this thesis was to investigate and elucidate how light, administered by standard ceiling mounted LED-luminaires, can be used to facilitate adaptation to night work on measures of subjective alertness, performance, and circadian rhythm.

1.1 Working time and shift work charachteristics

The organization of the working time may impact workers' health and quality of life. For instance, it is well-known that certain working time arrangements, such as shift work, can negatively impact workers health [4]. Furthermore, shift work entails non-standard work hours which may also impact workers' social life (e.g. work-family balance) [12]. As working time has been recognized as an important factor for workers health, most countries have legislations that regulate working time arrangements to protect the health of workers. In Norway, working time is regulated in the Working Environment Act, while in European countries the regulations are under the European Working Time Directive [13]. These regulations provide specific rules regarding e.g. the length of working time and minimum rest periods. As an example, in every 24-hr period a worker is entitled to a minimum consecutive rest period of 11 hrs, and in case of night work the average working hours must not exceed 8 hrs per 24-hr period.

While most of the workforce are engaged in regular day work, with the work periods falling somewhere between approximately 07:00 and 17:00 hrs, many workers are engaged in irregular work hours or shift work. However, the term 'shift work' is not a precise concept as all types of working hours that takes place outside standard working hours, i.e. non-daywork, may be referred to as shift work [14]. Commonly, a

distinction is made between permanent shift work (e.g. permanent evening or night shifts), rotating shift work (e.g. alternating between morning, evening, and night shifts), and roster work (irregular types of rotating shift work) [14]. In the 2017 update of the sixth European working conditions survey, it was found that about 21% of workers reported shift work [2]. It is most common in the health sector where 40% are engaged in shift work. The most prevalent type of shift work is rotating shift work followed by permanent shift work [2].

Rotating shift work is usually divided in three-shift rotation or two-shift rotation systems. Three-shift rotation implies that workers rotate between morning, evening, and night shifts, while in two-shift systems, workers alternate between two of the shifts. Another type of two-shift rotation involves 12-hr shifts, alternating between day and night work [15]. Rotating shift work can also differ in terms of the speed (i.e. number of shifts before rotation) and the direction of the rotation. Forward rotation entails clockwise rotation (i.e. morning to evening to night shift), while with backward (counter clockwise) rotation the shifts may be scheduled as moving from night to evening to day shift. The latter, i.e. moving from an evening shift directly to a morning shift the following day, may cause restricted time to rest (< 11 hrs between consecutive shifts) between the shifts. Such rapid rotations have been termed quick returns [16]. In terms of speed, a schedule with one to three consecutive shifts of the same type before rotation has been considered to be fast-rotation, while at least five consecutive shifts of the same type before rotation have been considered to be a slow-rotating shift schedule [17]. Thus, a range of different shift work schedules exists, and in addition to the descriptions above, shift work can be described also according to dimensions such as continuous or discontinuous (every day of the week or no work in the weekends), length of the shift cycle, duration of individual shifts, start and end times of the shifts, number and position of rest days, regularity of schedules, and type of shift work (with or without night work) [18].

Night work

Night work has been referred to as a type of shift work where most of the working hours takes place between 21:00 and 08:00 hrs [19]. Others have noted night

work as shifts where ≥ 3 hrs takes place between 24:00 and 06:00 hrs [15], or that the start times of the shift is between 18:00 and 04:00 hrs [20]. In the Norwegian Working Environment Act, night work is defined as work taking place between 21:00 and 06:00 hrs. While there is no strict definition, night work implies that workers are being called for work duties at night when they would normally sleep.

In Europe, approximately 19% report work during the night at least once a month [2]. In the US, 7.4% of the working population were estimated to perform night work more than 5 times in the past 30 days [21]. For many workers, night work comes as part of a rotating shift work schedule, while in some sectors permanent night work is also prevalent. For example, in a US sample of healthcare workers, 19% worked permanent night shifts [22]. In investigations of the total workforce in Western countries, about 4% of employees have been reported to work permanent night shifts [20, 23]. Although some workers have a permanent night work schedule, it has been noted that nearly all shift workers can be considered as rotating shift workers, since most rotate back to daytime wakefulness during days off [20]. In the health sector, e.g. among nurses, night work typically comes as part of a three-shift rotation schedule, where it is common to work three consecutive night shifts [24].

Sleep deprivation

Night work often entails sleep deprivation or extended wakefulness (i.e. cumulative wakefulness > 16 hrs). It is common to distinguish between three types of sleep deprivation (SD), short-term total SD (≤ 45 hrs), long-term total SD (> 45 hrs), and partial SD (< 5 hrs sleep in a 24-hr period) [25]. Total SD may also be referred to as acute SD. In terms of night work, short-term total SD or extended wakefulness may occur especially during the transition from day shifts to night shifts [26, 27]. For instance, a worker may wake up at 08:00 hrs on the day before the first night shift, remain awake until and during the night shift (e.g. from 23:00 to 07:00 hrs), and fall asleep at 08:00 hrs on the next morning. Thus, this worker experiences a short-term total SD of 24 hrs, or 8 hrs of extended wakefulness. However, many workers nap in the afternoon before the first night shift, with the prevalence of napping reported to be

30–50% [5]. It is likely that some shift workers also experience partial SD due to shortened daytime sleep after a night shift [28], or in relation to quick returns [16].

1.2 Night work and health

Shift work has been associated with a range of health problems, and the main concern relates to disturbance of circadian rhythms, and sleep disturbances due to the non-standard work hours [4]. In the International Classification of Sleep Disorders [29], shift work disorder is one of five circadian rhythm sleep-wake disorders. Circadian rhythm sleep disorders are in general caused by a misalignment between the endogenous circadian rhythm and the external day-night cycle [30]. Shift work disorder is characterized by complaints of insomnia or excessive sleepiness, which can be attributed to misalignment of the individuals' circadian rhythm and the work schedule [20]. Especially night work may impact sleep, and among nurses involved in night work, studies have suggested that the prevalence of shift work disorder can be as high as 44% [31]. Evidence has also suggested that night work impact workers health in terms of increased risk for a range of health problems and diseases. This includes breast cancer [32], with some suggested mechanisms being related to disturbance of the circadian system, alteration of the light-dark schedule, and inhibition of melatonin production [33-35]; coronary diseases [36], possibly due to increased psychosocial-, behavioural- and physiological stress [37]; diabetes [38]; and gastrointestinal disorders [39]. In addition to long-term health effects, night work has immediate impact on workers' sleepiness/alertness, and performance [6, 27, 40, 41]. Such alertness and performance deficits have been related to the increased risk of injuries and accidents during night work [7, 42, 43]. Furthermore, sleep problems in general have been found to increase the risk of work injuries [44].

Models of shift work and health

There are many pathways and mechanisms that may contribute to the explanation of why night work is associated with adverse health outcomes. Several general non-specific (in terms of disease) models of shift work and health have been proposed based on existing empirical evidence [4, 45, 46]. These models have in

common that circadian disruption (i.e. disturbance of biological timing) and sleep disturbances are considered core processes for linking shift work and health problems. The latest model, proposed by Kecklund et al. [4], shows how shift work related behaviours may lead to chronic disease as well as acute cognitive impairments and accidents (**Figure 1**). The authors have identified pathways by which shift work leads to 1) circadian disruption, 2) disturbed sleep, and 3) risk behaviours and psychosocial stress. These components are bidirectional and interact with each other, and through physiological and psychological mechanisms, may cause chronic diseases and accidents [4].

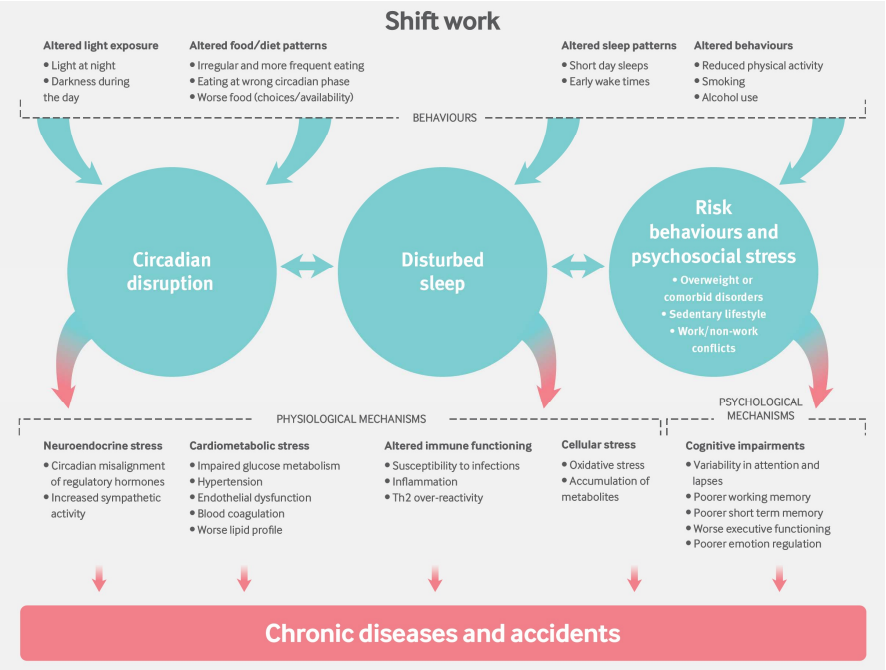

Figure 1 Theoretical model of mechanisms and pathways by which shift work and shift work related behaviours increase risk for chronic disease and accidents [4]. Reproduced from [Health consequences of shift work and insufficient sleep, Kecklund G, Axelsson J, 355, i5210, 2016] with permission from BMJ Publishing Group Ltd.

1.3 Circadian rhythms

The main reason for the health problems associated with night work relates to the conflict between the non-standard work hours and the workers' endogenous circadian rhythm [5], causing circadian misalignment. Circadian rhythms are reflected in biological processes displaying oscillations with a rhythmicity around 24 hrs. Such rhythms are considered to result from evolutionarily adaptation and regulates when biological events occur in relation to the 24-hr day-night cycle defined by the earth's rotation [47]. Circadian rhythms exist at a cellular level in peripheral tissues [48], but the peripheral cellular 'clocks' are controlled and coordinated by the suprachiasmatic nuclei (SCN) in the hypothalamus [49, 50]. The SCN serves as the primary circadian pacemaker, synchronizing the peripheral clocks to ensure proper functioning of the circadian system [51]. Like the peripheral cells, the SCN and individual SCN cells produces their own autonomous circadian rhythm [51-53]. The cellular clocks consist of a complex system of interacting positive and negative transcriptional feedback loops that generates rhythmic transcription of clock genes in the cells [54]. Light is known to regulate the expression of e.g. the mammalian period circadian regulator (*PER)* genes in the SCN, with photic induction of *PER1* being the primary stimulus for resetting the circadian clock [54]. In humans the circadian period has been estimated to have an intrinsic period of about 24.2 hrs on average [55]. Thus, the SCN needs to be entrained by external time cues to remain aligned with the day-night cycle.

Circadian rhythms can be seen in a range of different bodily functions. Most prominently is the sleep-wake rhythm, but also alertness and cognitive performance, core body temperature, and hormone production show circadian rhythmicity [1]. An example of the circadian rhythm of the core body temperature (CBT) can be seen in **Figure 2**. Despite continuous fluctuations in temperature a clear circadian pattern occurs, with the CBT being lowered in the evening and at night. Temperature and sleep are related processes, and the decline in CBT in the evening promotes sleepiness and initiation of sleep [56, 57]. In **Figure 2** the circadian minimum (nadir) of the CBT occurs at about the same time in every 24-hr period. On the third morning the CBT quickly rises as the subject was forced to wake up earlier than usual.

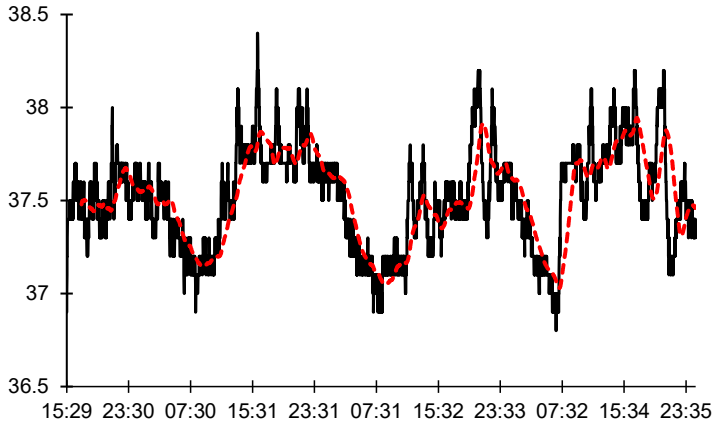

Figure 2. Core body temperature (°C) measured every minute (black solid line) over three days for one subject, using a BodyCap e-Celsius (BodyCap, France) temperature capsule. The red dashed line indicates the moving 2-hr average.

As a rule of thumb, the nadir of the CBT is located around 2 hrs before habitual wake time [30], hence for a person waking up at about 07:00 hrs every day, the nadir of the CBT could be estimated to occur at around 05:00 hrs. The time around the nadir of the CBT has been identified as the time with highest sleep propensity [57], i.e. the time it is most difficult to stay awake. Thus, night workers and subjects exposed to total SD experience high levels of sleepiness especially in the early morning hours close to the nadir of the CBT [58]. There are substantial individual differences in the timing of the circadian system, which impacts daily variation in human behaviours e.g. timing of sleep. Hence, people can be placed on a continuum from extreme morning types (i.e. 'larks') who prefer to wake up very early, to the opposite comprising extreme evening types (i.e. 'owls') who prefer to go to bed late at night [59].

Circadian entrainment

Several external factors may function as time givers (zeitgebers) for the circadian system, e.g. the timing of sleep plays a role, and also exercise, social cues, clock time, and food ingestion provide time cues to the circadian system [60]. However, the primary zeitgeber for synchronizing the internal circadian system is the light-dark cycle [61]. The SCN receives photic input from specialized intrinsically photosensitive retinal ganglion cells (ipRGCs), that signal directly to the SCN via the

monosynaptic retinohypothalamic tract [62]. The signals from the ipRGCs are non-image forming (i.e. nonvisual), hence circadian responses can be seen also in blind humans with intact inner retinal function [63]. The ipRGCs express the photopigment melanopsin which is maximally sensitive to short-wavelength blue light [64-66]. However, the ipRGCs also receives indirect light input from the rod and cone photoreceptors [67].

The SCN communicates to the peripheral clocks and cells both via neuronal and endocrine signalling. Of particular interest, the SCN regulates the production and release of the pineal hormone melatonin, which increases sleep propensity in humans and signals the time of day to peripheral tissue [68, 69]. SCN activity inhibits melatonin synthesis, hence melatonin is normally produced during the biological night. However, exposure to light at night supresses melatonin production [70]. This process is also mainly driven by the ipRGCs, and as for SCN entrainment, the melatonin suppression is most sensitive to blue light [71, 72]. Melatonin also provide feedback directly back to the SCN and inhibits SCN activity [73]. Thus, exogenous melatonin increases sleepiness in humans, and can shift the phase of the circadian rhythm if suitably timed [74]. As such, both light and melatonin can be administered as means for shifting the phase of the circadian system, and phase response curves (PRCs) for light and melatonin have been derived as shown in **Figure 3**.

Light administered in the ~ 9 hrs before nadir of the CBT phase delays the circadian rhythm, while light exposure during the ~ 9 hrs after nadir of the CBT phase advances the rhythm [75, 76]. In terms of exogenous melatonin, the PRC is approximately opposite than for light, as melatonin administered in the evening phase advances the circadian rhythm, while melatonin in the morning phase delays the rhythm [77]. In general, the phase shifting response is larger in the hours close to the nadir of the CBT [78], as seen in **Figure 3** the response to light peaks around 4 hrs before and after nadir of the CBT [75]. The endogenous circadian period length is normally slightly longer than 24 hrs, hence artificial environments free of zeitgebers cause free-running and gradually phase delay of most human's circadian rhythm [55]. Consequently, it is usually easier to phase delay than to phase advance the rhythm.

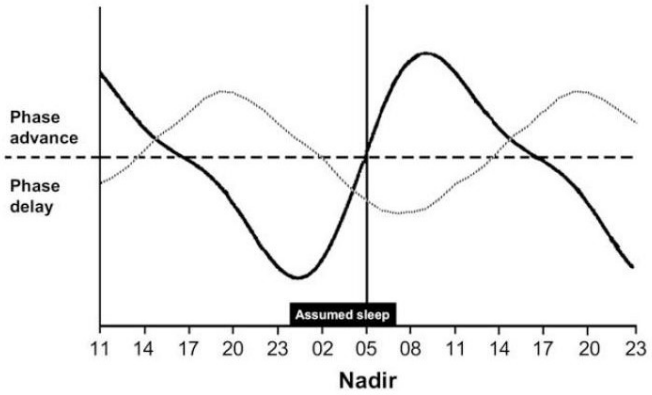

Figure 3. Phase response curves for light (dark line) and melatonin (light dotted line). Based on the results reported by Khalsa et al. [75] and Lewy et al. [70].

While circadian rhythms can be assessed by measuring the CBT, it is also possible to measure the endogenous melatonin rhythm, which is considered a reliable marker of the phase of the SCN [79]. Generally, the circadian phase is determined based on melatonin samples and estimation of the dim light melatonin onset (DLMO) [30]. As melatonin production is directly driven by the SCN timing [74], it is possible to monitor phase shift of the central clock on a day-to-day basis, e.g. for investigation of night workers circadian adaptation. Note that evidence suggests large differences in the rhythms of the SCN and the peripheral oscillators following simulated night work [80]. To estimate DLMO several melatonin samples in the evening, when melatonin level is rising, are required (usually at 30- or 60-min intervals). Commonly, DLMO have been defined as the time melatonin levels reaches 3 or 4 pg/mL in saliva [81, 82]. Ideally, for measuring circadian rhythmicity in e.g. melatonin and CBT, a constant routine protocol should be employed [83]. However, the constant routine is a comprehensive and demanding procedure for both researchers and participants, and the constant routine involves total SD which affect participants. Thus, restricting melatonin sampling to the evening, when melatonin levels are usually rising, can be preferable for estimating DLMO in practical/naturalistic contexts. Sampling at home can be applied, although it is common to encounter difficulties in estimating DLMO based on at home sampling, for instance due to melatonin suppression or participants mixing up samples [82].

Night workers and circadian adaptation

Considering the circadian entrainment induced by external zeitgebers, e.g. light exposure, night workers might be expected to phase delay their rhythm and gradually adapt to a night work schedule. Timed bright light and darkness have been shown able to induce near complete phase shift of the circadian rhythm within two to three days in highly controlled laboratory conditions [84]. However, adaptation in real-life takes time, and within 1–3 night shifts significant adaptation is usually not achieved [85]. In general, the circadian rhythm is considered to adjust about 1 hr per day, mainly due to duly timed light exposure [5]. Thus, with favourable conditions it would still take many consecutive night shifts before full circadian adaptation may be achieved. Work schedules with many consecutive night shifts or permanent night work may be argued to be beneficial in terms of allowing circadian adaptation. However, limited circadian adaptation was reported after seven consecutive night shifts [86], and even among permanent night workers only 21% showed substantial circadian adjustment, while 4% achieved full adaptation [87]. One explanation for the limited circadian adaptation relates to light exposure occurring not only during the phase delay part of the PRC, but also in the hours after the nadir of the CBT counteracting circadian adjustment. Studies have found that offshore workers on oil rigs in the North Sea tend to adapt well to night work schedules after 5–7 days with night work [88-90]. One probable reason is that offshore workers do not have to commute home after the night shift, hence they are not exposed to the same amount of morning daylight as onshore night workers. Additionally, they do not have to attend to domestic responsibilities while offshore. On the other hand, offshore workers seem to have problems readapting to a day-oriented schedule offshore [89], or when returning home [88]. Gibbs et al. [89] reported that there were very large individual variations in terms of adaptation and suggested differences in individual light exposure as a possible explanation. A recent study among healthcare workers engaged in rotating shift work (onshore), reported large inter-individual variability in the direction and magnitude of phase shift after three or four consecutive night shifts [91]. While most participants phase delayed from baseline to the final night shift a substantial portion of the workers phase advanced. Interestingly, the timing of light exposure relative to individuals' circadian phase, and

diurnal preference accounted for 71% of the variability in the circadian response to night work [91]. In sum, evidence indicates that night workers experience circadian misalignment and limited circadian adaptation to the night work schedule. These findings seem to apply to both rotating and permanent night workers. However, as noted, there are large variations in individual workers circadian response to night work, and timing of light exposure apparently has the potential to induce circadian adaptation if timed properly.

1.4 Sleep

Due to the circadian misalignment seen among night workers, i.e. altering the sleep-wake rhythm, sleep is highly affected by night work. Humans spend about one-third of their life asleep, yet the functions of sleep are not fully understood. Several hypotheses have been suggested, such as the importance of sleep for learning, memory, synaptic plasticity, brain energy metabolism, and removal of metabolic waste [92]. Although the functions of sleep need further elucidation, it is beyond doubt that sufficient sleep is essential for health and proper functioning [93].

Sleep can be defined as a 'reversible behavioural state of perceptual disengagement from and unresponsiveness to the environment' [94]. Despite the decreased responsiveness the brain is still active during sleep. Two main sleep states exist, rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep. Based on the electroencephalogram (EEG), the NREM sleep is further divided into N1, N2, and N3 according to the American Academy of Sleep Medicine [95]. The EEG activity in N1, N2, and N3 is characterized by alpha (8–14 Hz) and theta (4–8 Hz) activity; sleep spindles (7–15 Hz) and K-complexes; and delta (1–4 Hz) oscillations, respectively [96]. As seen in **Figure 4**, a healthy young adult normally enters sleep in NREM beginning with N1 and progressing through the deeper stages N2 and N3, with N3 also referred to as delta sleep or slow wave sleep, before the brain is reactivated with transition into REM sleep [94].

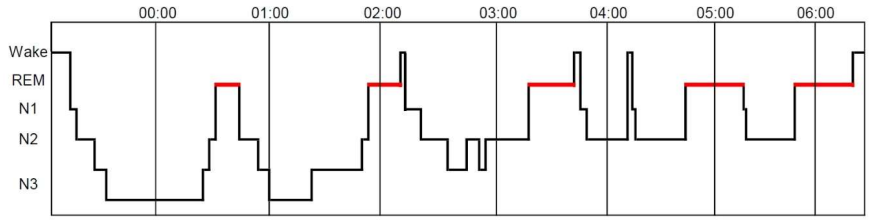

Figure 4. A hypnogram showing an example of normal distribution of sleep stages. The numbers on top indicate clock time.

While NREM sleep can be termed quiet sleep, REM sleep is characterized by EEG activation, muscle atonia, and episodes with rapid eye movements [94]. Throughout the night, NREM and REM sleep alternates with a period close to 90 min, with N3 dominating the first third of the night and REM sleep dominating the last third of the night [94]. In terms of sleep duration, young adults usually report to sleep around 7.5 and 8.5 hrs per night during weekdays and weekends, respectively [94, 97]. There are large differences in how much sleep individuals need. However, it has been recommended that the appropriate sleep duration for adults (18–64 years) is between 7 to 9 hrs [98].

The gold standard for measuring sleep is polysomnography (PSG), requiring at least recording of EEG, electromyogram, and electrooculogram signals to make proper distinction between sleep stages [99]. However, PSG is usually performed in a sleep clinic/laboratory (ambulatory PSG is also possible) and sleeping with PSG equipment may disturb sleep (e.g. first night effects). Thus, it is also common to use actigraphy [100] and self-report/sleep diaries [101] to monitor and quantify sleep and sleep quality. Actigraphy and sleep diaries allow for assessment of sleep in a more natural environment, require far less resources, and are less invasive than PSG. Actigraphy and sleep diaries do however not allow for sleep staging, but in many circumstances, it may be sufficient to assess parameters such as timing and duration of sleep. While sleep diaries provide a subjective sleep assessment, actigraphy is considered a more objective measure. Actigraphy measures limb movement, which is used to assess activity-inactivity as a proxy for wake-sleep. Actigraphy allows monitoring of wake-

sleep patterns over many days, and even years [102], hence actigraphy is suitable for investigating treatment effects, and circadian rhythms [100].

1.4.1 Sleep-wake regulation

The alternation between sleep and wakefulness is regulated by a complex network of brain circuitry. The ascending arousal system, a network of cells groups originating in the brainstem projecting to the thalamus and cortex, promotes wakefulness, while during sleep the ventrolateral and median preoptic nuclei in the hypothalamus inhibit the arousal system [103, 104]. Activity in the SCN, i.e. the circadian pacemaker, inhibits the ventrolateral preoptic nuclei mainly by indirect (via the dorsomedial hypothalamic nuclei) projections [62]. The wake promoting and sleep promoting neurons are mutually inhibitory, providing sharp transitions between sleep and wakefulness, avoiding transitional states [104]. However, Saper et al. [104] noted that unwanted transitions may occur, e.g. falling asleep (microsleep) during a momentary attentional lapse while driving [105].

The sleep-wake cycle has been proposed to be regulated mainly by two interacting processes, a homeostatic process and a circadian process, as conceptualized in the two-process model of sleep regulation [106, 107]. The sleep dependent homeostatic process entails that the need for sleep increases during time in wakefulness and decreases during time in sleep [106]. Hence, both total SD and partial SD increases the homeostatic sleep pressure, which can be seen in increased sleep propensity (i.e. sleepiness and reduced sleep onset latency) [99]. During sleep, the amount of N3 sleep mark the homeostatic process, with increased time in N3 after SD and reduced time in N3 during sleep after daytime napping [108]. The circadian process relates to the rhythmicity in sleep propensity generated by the circadian system and is mainly sleep independent [106], although it has been suggested that increased homeostatic sleep pressure attenuates the circadian system's responses to zeitgebers [109]. Circadian rhythms in sleep propensity have been demonstrated in experiments of total SD, where circadian rhythmicity in both subjective sleepiness ratings and cognitive performance can be seen [110, 111]. Also, forced desynchrony protocols, i.e. scheduling subjects to artificial day lengths deviating from 24 hrs, can be applied to

investigate circadian rhythms [112]. As the homeostatic and circadian processes interact, the optimal timing of sleep is considered to occur when the circadian drive for sleep is synchronized with elevated homeostatic sleep pressure [107], that is, during the biological night after a full day (i.e. 16 hrs) awake.

Although the two-process model provides a useful framework for understanding sleep regulation, other factors are also contributing to sleep-wake regulation. Behaviour can override both the homeostatic and circadian processes, and enables people, e.g. a night worker, to stay awake during a night shift [30]. Exposure to environmental factors such as light are also contributing, i.e. by eliciting acute alerting effects [10], and by its impact on the circadian system as described previously. Light exposure may also affect subsequent sleep, e.g. it was reported that, compared to dim light, light exposure (photopic illuminance = 250 lx) during 40 hrs of extended wakefulness increased the homeostatic sleep response [113]. Other environmental factors affecting sleep include noise [114], ambient temperature [115], as well as the quality of the bedding.

Night workers' sleep

As most night workers show limited circadian adaptation, when they go to bed in the morning hours, the circadian system promotes wakefulness [116]. This circadian misalignment challenges night workers' sleep, and accordingly night workers sleep less, and experience greater sleepiness compared to day workers [19, 117]. The circadian process mainly affects the duration of sleep, while the homeostatic process is considered to regulate how deep sleep is [30]. As the homeostatic sleep pressure is high due to extended wakefulness, most night workers tend to have short sleep onset latency and quickly enters N3 sleep, but sleep duration is usually shortened by 2–4 hrs between night shifts [28]. Due to N3 sleep mainly occurring and dominating the first parts of the sleep period, night workers' N3 sleep is marginally affected by the shortened sleep duration [118], but N2 and REM sleep duration are clearly reduced [5]. Recent studies found that total sleep time, measured using actigraphy between consecutive night shifts, was around 5.7 hrs among nurses and healthcare workers on rotating shift work schedules [6, 27]. These studies indicated that total sleep time

between consecutive day shifts did not differ from the night shifts. However, prior to the first night shift, evening shifts, and days off, total sleep time was around 2 hrs longer than between the consecutive day and night shifts. The shorter sleep duration prior to day shifts was suggested likely due to early day shift start times, resulting in truncated sleep [6, 27]. The sleep duration between consecutive night shift is clearly much shorter than the recommended 7–9 hrs for adults [98]. Åkerstedt [5] noted that to compensate for the shortened daytime sleep, about one-third of shift workers add a late afternoon nap between subsequent night shifts.

1.5 Night work, sleepiness and performance

It is assumed that the quality of wakefulness relates to the quality of sleep [99]. As such, evidence has shown that lack of sleep, both due to total SD and partial SD, have major implications for alertness and performance during wakefulness [119]. Night workers' daytime sleep may be shortened and lead to partial SD, while during night shifts workers may experience total SD. Thus, night workers experience increasing sleepiness throughout the night shift [120], and especially at the end of the shift during the early morning hours (close to the nadir of the CBT), the sleepiness levels and performance impairments are high [6, 27, 40, 41, 58]. Both circadian and homeostatic processes contribute to sleep-wake regulation, and as such also the increased sleepiness and performance impairments evident in the later parts of a night shift.

Sleepiness

Sleepiness is a universal phenomenon expressed both as a symptom of sleep disorders and as a normal physiological state. Sleepiness relates to sleep propensity, i.e. the tendency to fall asleep [121]. In clinical settings the Multiple Sleep Latency Test is an established measure of objective sleepiness, assessing how long it takes for a subject to fall asleep (using PSG recordings) during nap opportunities [122]. Physiological sleepiness may also be indicated by increased alpha and theta activity in the waking EEG, and by an increase in slow eye movements [123]. As it is demanding to carry out the Multiple Sleep Latency Test and/or EEG monitoring, it is also

common to use subjective measures for assessing sleep propensity, e.g. the Epworth Sleepiness Scale [124]. It has been suggested that sleep propensity or objective sleepiness should be distinguished from subjective sleepiness, as the latter is a perceived state correlated with various sleep related variables such as decreased cognitive performance, mood and a general sleep need [121]. It has also been suggested a distinction between manifest sleepiness, i.e. measurable behaviour indicating sleepiness (e.g. vigilance tests), and physiological sleepiness as measured by EEG [125].

Subjective sleepiness (i.e. state sleepiness) implies that wakefulness can be quantified in terms of quality on a sleep-wake continuum. The construct is sometimes considered the converse of alertness and is commonly measured using Likert scales, e.g. the Stanford Sleepiness Scale [126], and the Karolinska Sleepiness Scale (KSS) [123]. Subjective sleepiness level shows a clear diurnal pattern with high sleepiness in the morning, low sleepiness during daytime, and rising sleepiness levels in the evening [58, 127]. Åkerstedt et al. [123] demonstrated that subjective sleepiness, as assessed with the KSS, is also reflected in the waking EEG. Corroborated by other studies showing that subjective sleepiness rating is closely related to both EEG and behavioural alertness (vigilant attention) variables [128], subjective rating scales are considered as valid measures of sleepiness. Partial SD studies have shown that under conditions with sustained sleep restriction, daily subjective sleepiness level is increased but stabilizes, while vigilant attention deficits steadily build-up from day-to-day [119]. Thus, in such circumstances the subjective sleepiness level may not reflect or correlate with task performance.

As subjective sleepiness scales are easily administered it is a common method for assessing sleepiness, i.e. state of wakefulness/alertness, during night work and SD studies. The increased subjective sleepiness evident during night work, has been associated with decreased cognitive functioning and performance (e.g. driving) among night workers [27, 129]. Furthermore, sleepiness has been associated with increased risk of accidents and injuries during night work [7, 130-132]. Major disasters including Chernobyl, Exxon Valdez and the Three Mile Island accident occurred at night and

have anecdotally been related to sleepiness [131, 133]. Although subjective sleepiness scales provide useful measures of the wakefulness/alertness state, they should ideally be accompanied by other measures, e.g. alertness assessed with cognitive performance tasks.

Performance

A large number of studies have assessed how sleep loss, both total SD and partial SD, may affect various cognitive domains and performance tasks [134-136]. In general, there is a slowing of response times (RTs) and increased variability in performance during SD. However, it has been debated whether such impairments affect all cognitive capacities in a global manner, or if SD may also have selective/specific effects on certain brain areas, i.e. specific cognitive capacities [134, 135]. The latter approach was endorsed by Horne [137], suggesting that SD especially impairs cognitive capacities relying on the prefrontal cortex, including higher order executive functions such as complex decision making [138]. Indeed, studies have shown that both total SD and partial SD impairs decision making capacities, relying heavily on the prefrontal cortex, such as moral judgement and reasoning [139, 140]. Harrison et al. [138] further suggested that performance degradation on simpler tasks is mainly due to boredom. On the other hand, in support of a global effect of SD on cognitive performance is the assumed hierarchical order of cognitive capacities, where higher order capacities to some degree rely on more basic functions. For instance, a certain level of alertness is required for engagement in complex decision making. By assessing SD effects on several neurobehavioral tests, Van Dongen et al. [141] reported three dimensions of neurobehavioral deficits due to SD, indicating that distinct neurocognitive systems may mediate the cognitive effects of SD. Interindividual differences in impairment differed across tasks, and cognitive processing capability and sustained attention was affected differently [141]. Thus, it was suggested that operational tasks depending on sustained attention, e.g. monitoring of automated systems in a control room, may be affected differently than brief performance tasks depending on cognitive processing capabilities [141]. Indeed, studies have found that the most consistent cognitive impairment during SD, is seen on basic capacities, i.e. sustained/vigilant attention [142, 143].

Circadian rhythmicity has been indicated for various cognitive performance tasks, mainly however in vigilance and attention parameters [144]. Scmidt et al. [144] noted that assessing circadian rhythms in higher order capacities is difficult, as tests of executive functions usually shows practice effects and require some form of novelty. It has been indicated a close relationship between CBT (which have a clear circadian rhythm) and a variety of performance measures [145]. In terms of sustained attention, circadian rhythmicity in performance can be seen both on RTs and errors on psychomotor vigilance tests [146, 147].

Vigilant attention/alertness

It has been argued that alertness is not the opposite of sleepiness, and that alertness refers to a person's ability to respond to external and internal stimuli [148]. Thus, a person reporting a high level of sleepiness may still be somewhat alert and able to respond to stimulus, hence alertness can be quantified by assessing that ability. Such behavioural alertness is often measured using simple performance tasks assessing vigilant attention, i.e. the ability to maintain focused attention over a period of time by responding to visual or auditory stimuli in a timely fashion [149]. Due to its sensitivity to sleep loss and its psychometric properties [143, 150], the Psychomotor Vigilance Task (PVT), originally developed by Dinges et al. [151], has become the gold standard for assessing vigilant attention in SD studies.

The vigilant attention/alertness impairment during SD relates to the time-on-task effect, or vigilance decrement, which posits worsening of performance (i.e. timely or correct responses) across task duration [152]. As for sleep-wake regulation, vigilant attention is driven by homeostatic and circadian processes. Doran et al. [147] reported that performance deficits increase with increasing homeostatic sleep pressure, performance is however partly restored in the afternoons due to circadian processes promoting wakefulness/alertness at this time. A third allostatic process has been suggested to also regulate the temporal dynamics of vigilant attention, and a range of other factors such as light exposure, physical activity and distractions influence vigilant attention [149]. In addition, there are large individual differences in the vigilant attention deficits seen under both total SD and partial SD, and these inter-

individual differences are considered to reflect a trait-like vulnerability [141, 153]. Furthermore, it has been suggested that individuals are not capable of accurately self-estimate their vulnerability to sleep loss, as there is a discrepancy between individual differences in behavioural alertness and individual differences in subjective sleepiness during SD [154].

The performance deficits seen on vigilant attention tasks during SD are characterized by increased moment-to-moment variability, and already in the 1950's such observations lead to the lapse hypothesis [155]. The lapse hypothesis implies that task performance during SD for the most part is unaffected/normal, but disrupted by brief periods of reduced responsiveness, i.e. a lapse. Hence, if a stimulus on a task coincide with the occurrence of a lapse, the response will be delayed or omitted. While increased number of lapses is evident during SD, there is also a general slowing of RTs and it has been suggested that SD leads to wake state instability [147]. Wake state instability entails that SD performance is unstable due to the interaction between homeostatic pressure for sleep, circadian pressure for wakefulness and compensatory efforts to uphold performance. According to the wake state instability hypothesis, there are rapid fluctuations between wake and sleep during SD, leading to a variability of performance, especially on vigilant attention tasks [147]. It has also been proposed that local sleep may explain the vigilant attention deficits evident during SD, suggesting that neuronal groups involved in a certain task may fall asleep locally due to sustained use [156]. This can explain the vigilance decrement during SD, seen on simple vigilant attention tasks relying heavily on specific brain circuitry. Hudson et al. [149] suggested that a rest/break or switching to another task not relying on the same circuitry may allow recovery from local sleep. Furthermore, differences in individual's specific brain circuitry capacity to process information may explain inter-individual differences in vulnerability to sleep loss [149].

The PVT have been used to assess night workers performance dynamics during night shifts. In general, the findings among actual night workers concur with the findings from experimental SD studies. Ganesan et al. [6] found that, among healthcare workers, both PVT RTs and number of PVT lapses of attention increased

from the start to the end of a night shift, while during day shifts PVT performance remained stable during the whole shift. Furthermore, Ganesan et al. [6] reported that PVT performance was equally impaired on subsequent night shifts. On the other hand, Magee et al. [157] reported that PVT performance during a simulated night shift, following 4–7 consecutive real-life night shifts, was more impaired compared to a simulated night shift following 2–3 consecutive real-life night shifts. In another simulated night shift experiment, it was also reported that PVT performance was impaired during night shifts, and although performance was worst on the first night shift, there were only minor differences between the subsequent night shifts, indicating limited adaptation [41].

1.6 Individual differences

It has been suggested that some individuals may have the ability to adapt to shift work without adverse consequences, i.e. having shift work tolerance [158]. Yet, there are no consensus on how to define or measure shift work tolerance, hence a range of different measures have been used to assess this, making comparisons between studies difficult [159]. Nevertheless, in relation to night work and SD both circadian responses, sleep disturbance, and impairment of alertness and performance, seems to be affected by individual factors [91, 141]. Typically, age, gender, personality traits and circadian preference have been investigated in relation to shift work tolerance [160]. Furthermore, research have investigated whether individuals' genetic variants affects adaptation to shift work, e.g. variants of clock genes [161].

Age

Young age is generally considered positive for shift work tolerance [159], but it has been noted that a few studies have suggested older age to be beneficial, e.g. in terms of risk of some diseases [160]. However, the latter notion is probably explained by the older shift workers being a selected group that cope well with shift work, i.e. healthy worker effect [160]. As noted by Ritonja et al. [159], virtually all health and sleep problems become more severe with age. One study indicated that night work before age 25 was associated with lower risk of shift work related diseases compared

to older age [162]. Another study reported that young workers had better circadian adjustment to three consecutive night shifts compared to older workers [163]. In terms of cognitive performance, ageing is generally associated with slower RTs among adults [164]. Interestingly, studies have shown that the RTs, and lapses of attention, among younger subjects increases during SD, while older subjects seem less affected [165-167]. This is particularly evident with sleep pressure related performance decrements, indicating that with > 16 hrs of wakefulness the age differences in adults RTs disappears, and young adults perform at a similar level as older adults [167]. On the other hand, a study of night workers indicated that older workers' performance (RTs and lapses) is more impaired compared to younger workers [168]. Also, a study of female hospital nurses, found that decreased cognitive performance, in terms of correct responses on a digit symbol substitution test and omission errors on a letter cancellation task, was associated with clock time, but also older age [129]. Bonnefond et al. [168] reported that the oldest (50–58 years) workers slept about 1 hr less than the youngest (25–34 years) workers after evening and night shift, but after morning shifts sleep duration was similar. It is known that older adults do not sleep as well as younger adults [169], and with aging the phase of the circadian rhythm becomes advanced [170], i.e. older adults tend to go to bed and wake up earlier than young adults. Thus, for night workers who have to sleep at unconventional biological times, age may further challenge sleep, and early chronotype has been associated with poorer sleep and sleep disturbance in connection with night shifts [171].

Gender

Male gender seems to be associated with increased shift work tolerance, although some inconsistency exists, depending on the measures used [159]. In a relatively small sample of experienced shift workers a trend for men adjusting faster than women, to three consecutive night shifts, was reported [172]. In a study of nurses, male gender was associated with a higher risk of shift work disorder compared to females [31], and one study suggested that long duration of exposure to night shift work is associated with increased mortality especially in male white-collar workers [173]. In general, women typically report poorer sleep quality, more sleep disruptions, and are at greater risk for insomnia than males [174]. Men have a more pronounced

preference for eveningness than women [175], and the intrinsic circadian period in women is shorter than in men [176]. However, studies have indicated that women's sleep occurs at a later biological time than in men, and that women have a stronger amplitude of the circadian variation in alertness with a larger decline around nadir of the CBT [177, 178]. As such, the performance of women tends to be more impaired in the early morning hours [179]. The abovementioned gender differences may contribute to women being more vulnerable to sleep problems, and not coping with night work and SD in the same way as men. Also, men are generally faster than women in terms of simple RTs, yet there are some differences in strategy, as women tend to prefer accuracy over speed, in contrast to men [167]. Noteworthy, studies have indicated that menstrual phase impacts performance especially at night near the nadir of the CBT [180]. Indeed, it was found that for women undergoing SD for at least 30 hrs, follicular-phase women had greater performance impairments than both luteal-phase women and males [181]. Follicular-phase women had a stronger amplitude of the variation in CBT than luteal-phase women, and compared with men, the luteal-phase women performed better in terms of PVT RTs and errors of commission [181]. It has also been suggested that family and domestic duties may challenge women's shift work tolerance [182].

Circadian preferences and personality traits

Chronotype or circadian type, is an aspect of individual differences in circadian rhythms, that places individuals on the morningness-eveningness dimension ranging from extreme morning types to extreme evening types, with most individuals being intermediate types. These differences can be seen in individuals' preferred timing of sleep and wakefulness, following a normal distribution in the population, with extreme morning types waking up at the time extreme evening types go to bed [183]. As noted previously, chronotype depends on both age and gender, tending to change from evening to morning preference with aging, and eveningness is more pronounced among men. In terms of shift work, evening types are suggested to have higher shift work tolerance, compared to morning types [159]. This is plausible as evening types go to sleep and wake up about 2 hrs later than morning types [184]. Assessment of alertness level at 08:00, 14:00, and 23:00 hrs, indicated that definitely evening types

have peak alertness at 23:00 hrs, while definitely morning types have peak alertness at 08:00 hrs [185]. It has also been found that the build-up of subjective sleepiness is slower in evening types compared to morning types [186]. In relation to night shifts, earlier chronotypes have shortened sleep duration, higher social jet lag, and higher levels of sleep disturbances [171]. Among shift working nurses, earlier chronotypes have lower adaptation scores for night shifts than later chronotypes [161]. On the other hand, a study of intensive care unit nurses working night shifts, did not find differences in sleepiness and PVT performance between morning and evening chronotypes [187]. However, morning type individuals were more likely to nap before commencing the night shift, compared to the evening types [187]. Interestingly, one study suggested that evening types are more susceptible to adverse light at night effects during night work, as chronotype was found to affect level and timing of melatonin production [188].

It has also been found that circadian type in terms of languidity (i.e. difficulty overcoming sleepiness) and flexibility (i.e. the ability to sleep at odd hours) may be related to shift work tolerance [189]. Among shift working nurses, high scores on languidity have been related to more sleep-wake disturbance in relation to night shifts, while flexibility was associated with higher sleep-related shift work tolerance [190]. Another personality characteristic, hardiness (i.e. resilience to experiencing negative stress), have been associated with shift work tolerance in terms of reduced sleep-wake disturbance during night shifts [190]. Furthermore, it has been suggested that extroversion is positively related to shift work tolerance, while neuroticism is related to low shift work tolerance [160].

Genetics

Genetics have also been investigated in relation to individual differences in shift work tolerance. Genetics and heredity have been associated with both circadian phenotype (i.e. chronotype), and variation in sleep duration (i.e. sleep need) [191]. Circadian gene variants are known to influence both sleep and waking function, i.e. cognitive performance, in relation to sleep loss [192, 193]. Furthermore, different genetic variants have been related to both sleepiness and insomnia among shift

workers [161, 194]. In terms of the trait-like vulnerability to effect of SD, a clock gene *PER3* length polymorphism has been identified as a bio-marker, with sleep and performance of $PER3^{4/4}$ homozygotes being less vulnerable/impaired by sleep loss and SD than $PER3^{5/5}$ homozygotes and $PER3^{4/5}$ heterozygotes [193, 195, 196]. Adenosine have been suggested to play a role in regulation of sleep homeostasis [197], and gene variants involved in adenosine regulation have been found to also impact performance during SD [198, 199]. In terms of PVT performance during total SD, a polymorphism in the TNFα gene (TNFα is involved in sleep-wake regulation) was found to explain 6.4% of the variance [200], and two genetic variants of the dopaminergic system explained 15% of variance in PVT performance [201].

1.7 Countermeasures

Night work is associated with adverse health outcomes, sleepiness/reduced alertness, reduced performance, as well as increased risk of accidents. Hence, several measures to counter the negative impact of night work have been suggested [8]. The most effective countermeasure would be to avoid night work completely. However, since night work is common, and in many sectors necessary, it is imperative to take measures that reduces the adverse effects of night work. Several approaches have been suggested, e.g. selection of shift work tolerant personnel, and arranging the shift work schedule in a favourable way, e.g. by using forward rotation and avoiding long shifts [8]. Other common countermeasures include napping during the night shifts [202], use of stimulants such as caffeine and/or bright light for enhancement of alertness and performance [203, 204], melatonin for improved daytime sleep [205], and various combinations of these countermeasures. While the aforementioned countermeasures may have beneficial effects for night workers, Smith et al. [206] noted that such measures may not address the underlying problem with night work, which is circadian misalignment. Furthermore, although many countermeasures may have beneficial effects on sleep and performance, there is less knowledge of the long-term health effects of countermeasures.

As the aim for this thesis is to investigate how light can facilitate adaptation to night work, in the following the focus will be on light, nonvisual responses, and how light exposure may be used as a countermeasure against the negative, mainly short-term, impacts of night work.

1.7.1 Light and nonvisual responses

Light is essential for vison, and in vertebrates, retinal photoreceptors (i.e. rods and cones) convey light information for vision to the brain via the optic nerve. For humans, the visible wavelengths of light ranges from around 400 nm (violet-blue) to around 700 nm (red), with peak spectral sensitivity for vision around 555 nm (green) [207]. However, light also elicits nonvisual responses via the ipRGCs, a third class of retinal photoreceptors. The ipRGCs project directly to the SCN, but also widespread throughout the brain, including to the ventrolateral preoptic nuclei [208]. Thus, in addition to modulate the circadian system, light exposure acutely affects e.g. sleep regulation and arousal, alertness, and cognitive processes [10, 209-211]. Neuroimaging studies, using positron emission tomography or functional magnetic resonance imaging, have been used to demonstrate that brain activity is modulated by light [210]. Perrin et al. [209] found that subcortical areas involved in alertness regulation, including regions encompassing the SCN and the ventrolateral preoptic nuclei, were affected by light during engagement in an auditory oddball task. Furthermore, light modulates brain activity, during nonvisual cognitive tasks, in alertness-related subcortical areas such as the brain stem [212]. In addition, structures typically involved in executive functions (complex cognitive tasks) are modulated by light exposure, and the effects are wavelength dependent (i.e. sensitive to short-wavelength blue light), differ between individuals, and depend on both homeostatic sleep pressure and circadian phase [213, 214].

The retinal photoreceptors have different wavelength or spectral sensitivity, i.e. the photopigment of ipRGCs, melanopsin, shows peak wavelength (λ_{max}) sensitivity at approximately 480 nm, rod opsin, the photopigment of rods, shows λ_{max} sensitivity around 500 nm, while the opsin of the three types of cones (S-cones, M-cones, and L-cones) have λ_{max} sensitivity around 420 nm, 530 nm, and 560 nm, respectively [215,

216]. Thus, when measuring light for nonvisual responses it's important to assess and report the spectral power distributions (380-780 nm), specifying the amount of energy (photons) at each wavelength, in order to estimate the stimulation of the different photopigments [215, 216]. Using only the common light unit lux/lx (photopic illuminance), which is basically a unit for assessing apparent brightness for the human eye, is thus not sufficient. For instance, if humans are exposed to monochromatic (narrowband) red light with λ_{max} at 625 nm and an illuminance of 40 lx, the stimulation of melanopsin (i.e. ipRGCs) would be close to zero. On the other hand, exposure to monochromatic blue light with λ_{max} at 455 nm, using the same illuminance (i.e. 40 lx), would induce substantial melanopsin stimulation. Note, that indirect light input from rod and cone photoreceptors also reaches the ipRGCs [67]. Thus, the nonvisual responses to light depend on properties of the light including intensity, spectral composition, timing, duration of exposure, and prior light history [217].

Bright light has been applied therapeutically for many years, and especially for treatment of circadian rhythm sleep disorders [30]. In addition, bright light has been applied as an effective treatment of depression [218], and in particular seasonal affective disorder [219]. In terms of nocturnal light exposure, dose-response relationships have been established for light intensity and alerting responses, melatonin suppression, and circadian phase shifting responses [220, 221]. With light exposure for 6.5 hrs, under carefully controlled laboratory conditions, half of the maximal alerting effect of light can be induced with illuminance around 100 lx, with saturation of alerting responses occurring with illuminance approaching 1000 lx [221]. Under similar exposure conditions, saturation of melatonin suppression occurs with illuminance around 200 lx (minimal suppression < 80 lx), while saturation of the phase shifting response occur with illuminance around 550 lx (little phase shift < 15 lx) [220].

As the nonvisual responses rely on the ipRGCs, responses such as melatonin suppression/regulation [71, 72, 222], pupil constriction [223], circadian phase shifting [224, 225], and alerting responses [222, 226], are sensitive to short-wavelength blue light. While short-wavelength monochromatic light elicits greater nonvisual responses

than monochromatic long-wavelength light, also short-wavelength enriched (i.e. blue-enriched) light may have similar properties, although findings are somewhat ambiguous [227-229]. It should be noted that light intensity may impact the responses to blue light. Short-wavelength blue light and blue-enriched white light seem to induce greater nonvisual responses especially under relatively low light intensity levels, while with higher light intensity the differences are less clear [230]. For instance, alerting effects of a 30-min bright light (> 1000 lx) exposure at 03:00 hrs, was seen both with polychromatic light and short-wavelength filtered light [231]. Also, using bright blue-enriched white light is no more effective than standard bright light in phase shifting the circadian rhythm [232, 233].

As previously described, the timing of light exposure is important for the circadian phase shifting response (i.e. phase delay or advance), and PRCs for timing of bright light have been derived [75]. Similarly, PRCs for monochromatic blue light has been established [234]. While these studies have used rather long duration (around 6.5 hrs) light exposure, it has also been established that short duration (0.2 hr) bright light exposure can phase delay the circadian pacemaker [235]. Chang et al. [235] derived duration-exposure curves for phase shift (i.e. PRC) and melatonin suppression, indicating non-linear relationships, e.g. a 0.2 hr light exposure was 5 times more effective (per min of exposure) in phase delaying the circadian pacemaker than 4 hrs of light exposure. However, increasing the exposure duration (from 1 to 3 hrs) to bright light with moderate (~ 2000 lx) light intensity increased the phase delay of the melatonin rhythm, while increasing from moderate to high (~ 8000 lx) light intensity did not increase the circadian response [236]. In practice, increasing the duration of exposure may thus be feasible.

Many of the controlled laboratory studies of light responses have applied some form of dark adaptation prior to light exposure, e.g. using dark glasses or dim light exposure. Indeed, prior light history (1 lx vs. 90 lx) was found to impact the direct effects of nocturnal light exposure (90 lx) on alertness, cognitive performance and waking EEG [237]. Thus, light deprivation before a light stimulus increases the efficacy of the light exposure.

In addition to properties of the light and light exposure, other factors also impact the nonvisual responses. A recent study revealed large interindividual variability in the sensitivity to light in terms of melatonin suppression [238], as the effective dose for 50% melatonin suppression was found to range from 6–350 lx in the most and least sensitive individual, respectively. One study found that the circadian system of patients with delayed sleep-wake disorder is more sensitive to light exposure (~ 150 lx), exhibiting 31.5% greater phase delay, than healthy controls [239]. Sex differences in responses to blue-enriched light in the evening have also been found, with males showing increased PVT performance (i.e. vigilant attention) during exposure, and increased slow-wave activity during NREM sleep after exposure, compared to females [240]. It has also been suggested that nonvisual effects depend on genotype, as blue-enriched light was found to suppress melatonin, induce alertness and attenuate theta activity in the waking EEG, in *PER3*$^{5/5}$ individuals, but not in *PER3*$^{4/4}$ individuals [241]. Similarly, functional magnetic resonance imaging showed increased brain responses to blue light during sleep loss in *PER3*$^{5/5}$ individuals only [213]. Thus, light exposure seems to be beneficial especially in those individuals vulnerable to sleep loss. It is also known that age comes with retinal changes, and it has been shown that the ability of light to impact the circadian system, both in terms of phase shifting responses and melatonin suppression, is reduced with older age [242, 243].

Light interventions and night work

In the early 1990's it was shown that bright light exposure during simulated night-work experiments could improve circadian adaptation to night work, and alertness and task performance during the night shifts [203, 244-246]. Based on simulated night work studies the principles for circadian adaptation among night workers, using light and dark exposure, have been elucidated [247]. The early studies of bright light and night work mainly used light therapy lamps, i.e. light boxes, for administering light, and dark sunglasses for limiting light exposure in the morning hours. In a field study among nurses, it was found that intermittent bright light exposure during night shifts, and dark glasses and bedrooms after night shifts (12 night shifts over 21 days) lead to complete entrainment of the circadian system to the night work schedule [248]. However, it has been noted that full adaptation may often not be

preferable, and a compromise has been suggested, i.e. partial entrainment aiming to delay the nadir of the CBT to occur during the daytime sleep episode after night shifts [247]. With this approach, the sleepiest time of the circadian rhythm is delayed into the daytime sleep episode, and such phase delay has been found beneficial for both night shift performance and daytime sleep [249].

While short-wavelength blue light has the potential to elicit greater nonvisual responses, the use monochromatic blue light during night work is rare. However, in one study using a driving simulator at night, exposure to dim narrowband blue light administered by a LED placed at the dashboard, suppressed EEG slow-wave delta and theta activity, reduced slow eye movements, and improved PVT RTs, compared to dim white light [250]. Blue-enriched light interventions have more commonly been used in connection with night work. Lowden et al. [251] found evidence that subjective sleepiness, among control room workers, was reduced during night shifts with blue-enriched light exposure in the beginning of the shift. Another study found that highly blue-enriched light (17000 K; 350 lx) improves control room workers' subjective sleepiness, working memory, and sustained attention during night shifts, compared to 350 lx of 3000-4000 K light and 6500 K light [252]. However, a study of night workers exposed to blue-enriched light (17000 K; 89 lx), compared to a standard light (4000 K; 84 lx), found no significant differences in alertness and performance during a simulated night shift [253].

Challenges/issues with light interventions

Although light exposure can induce nonvisual responses that may be beneficial for night workers, applying light interventions in real-life may be challenging. One issue concerns administration of light. Traditionally, bright light has been administered using light therapy boxes, e.g. in Bjorvatn et al. [254], thus requiring individuals to sit preferably unoccupied in front of the light box for a certain duration (typically 30–60 min). This allows for individually tailored light exposure which is beneficial considering interindividual differences in circadian rhythms and responses. However, in many occupations, requiring workers to sit in front of a light box may not be feasible. Another approach for providing light exposure is by using light therapy

glasses. A recent study found that light glasses were comparable with light boxes, in terms of effectiveness in counteracting effects of acute short-term SD in the early morning hours during a simulated night shift [255]. Specially designated light rooms have also been used to administer bright light, e.g. Lowden et al. [256] installed bright light facilities (ceiling mounted lighting) in the lunch/break room of night workers and found beneficial effects for the night workers. Lowden et al. [256] noted that using light rooms may be more cost-effective than installing such light facilities at the whole workplace. However, technological development has made cost-effective tuneable LED-luminaires available [11], and nowadays such lighting may be used to administer a variety of light conditions. Thus, it is now possible to administer light interventions via standard ceiling mounted LED-luminaires, without interfering with the work tasks or putting special requirements on workers.

A concern with light interventions for night workers relates to the possible adverse effects of nocturnal light exposure, i.e. artificial light at night. Light exposure may have beneficial effects for night workers, but disturbance of circadian rhythms and suppression of melatonin due to light at night, may also cause negative health effects [33, 257]. The International Agency for Research on Cancer has classified night shift work in Group 2A, 'probably carcinogenic to humans' [258]. One of several suggested mechanism for the probably increased risk of cancer is that light at night causes melatonin suppression, as melatonin is known to have e.g. antioxidative properties [259]. As such, it was reported that night workers have higher levels of oxidative stress and lower levels of antioxidant defences when compared to day workers [260], likely due to melatonin suppression. Thus, light interventions using short-wavelength depleted/filtered light, to avoid melatonin suppression, have been investigated (e.g. [231, 261-264]. These studies have indicated that filtered light have the potential to preserve melatonin levels during night shifts without having adverse effects on performance and sleepiness. On the other hand, exposing workers to various degrees of blue light (3000, 6500, and 17000 K light) during night shifts, did not reveal differences in antioxidant capacity, although melatonin concentration differed [265]. In general, the long-term effects of artificial light are not well understood but concerns regarding the long-term effects of blue light exposure have emerged. In a

recent study, Nash et al. [266] found that in Drosophila flies maintained in cycles of 12 hrs with blue LED and 12 hrs with darkness, the longevity was significantly reduced compared with flies maintained in constant darkness or in light with blue wavelengths blocked. Thus, there are indications of adverse effects of prolonged blue light exposure. For blue light exposure, concerns have also been raised regarding short-term effects in terms of potential photochemical damage to the retina, i.e. blue-light hazard [267]. However, a recent review reported that there is currently no evidence indicating that LEDs used at normal domestic intensity are dangerous to the human retina [268]. As such, commercially available LED-luminaires conforming with safety standards is not expected to pose acute risk for retinal damage. Still, long-term effects of blue light exposure from LEDs need to be further elucidated in humans, also in terms of potential retinal damage.

1.8 Methodological issues

In shift work research, including night work, experimental and quasi-experimental research designs have typically been used in real-life field studies to assess short-term effects [269, 270], e.g. immediate effects of interventions. Another similar approach is to conduct simulated shift work experiments under controlled conditions outside real-life work settings, such as in the laboratory [270]. The latter approach is very common in night work studies. A third approach in shift work research, not described in this thesis, is to analyse epidemiological data, and/or conduct cross-sectional and longitudinal survey studies [270], e.g. to investigate long-term health effects and changes over time. In experimental research designs the aim is basically to manipulate one variable while keeping all other variables constant. Thus, in night work experiments, it is important to consider and control confounding factors to be able to draw conclusions about causal relationships, i.e. internal validity. In field studies of shift work, controlling confounding factors is very difficult. Hence, by conducting simulated shift work in the laboratory, a major benefit is better control of potential confounders such as work schedule, work tasks, light exposure, diet, sleep, and chronotype [271]. Using a laboratory also allows for incorporating a constant

routine into the study protocol for assessment of circadian phase before and after night work, as in the study by Czeisler et al. [245]. With the constant routine it is possible to avoid biases that may affect the true endogenous rhythm, such as behaviours and environmental factors. Keeping subjects awake for > 24 hrs in constant dim light, with a fixed body posture and very low activity, and nutritional intake distributed evenly at day and night, allows for assessment of a full circadian cycle [83]. By using the constant routine with multiple nap opportunities, it is also possible to assess circadian rhythmicity with low impact of the homeostatic process and sleep pressure [112]. However, using the constant routine clearly affects the participants, and is a tedious and resource demanding procedure, thus it is often not feasible to incorporate in studies of night shift work.

A disadvantage with laboratory studies, compared to field studies, of shift work is of course that they are not performed under real-life conditions [271]. Thus, the external validity, i.e. the generalizability to a real-life workplace setting, may be limited. Yet another issue concerning external validity is that, while investigating actual shift workers in simulation studies is possible, it is more common to study shift work using samples of healthy young subjects with limited shift-work experience [271]. Evidence has suggested that experienced shift workers cope better with SD experiments in the laboratory than non-shift workers [272]. One likely explanatory factor contributing to such differences relates to the 'healthy worker effect', i.e. only the workers still engaged in shift work are studied, and not those who quitted due to not coping with the shift work schedule [270]. It has been shown that both light responses and cognitive impairments during SD and/or night shift work differ with age [129, 168, 243]. Thus, experiments using samples of young healthy participants, may not be generalized to other samples, e.g. older workers.

A basic standard experiment consists of two equivalent groups of participants, one experimental group, and one control group. Ideally, the only difference between the groups is the independent manipulated variable, e.g. the light conditions during night work. Different participants may be assigned to the two groups in a between subject's design, however, in night work and light experiments it is also common to

employ repeated measures design, i.e. individual participants complete all conditions (e.g. experimental and control condition). In a repeated measures design, fewer participants are needed, and a major advantage is that individual differences among participants can be accounted for. For instance, there are known individual differences in responses to SD, and light exposure [141, 238]. Still, repeated measures designs come with some methodological issues that need to be considered, such as the effects of the order of conditions, practice/learning effects, and carryover effects. Thus, the order of conditions needs to be counterbalanced, and the time between conditions should be sufficient for effects to wear off. To minimize learning/practice effects (i.e. with repeated administration cognitive tests) it is common to include a practice session as part of the experiment. Another problem with studies of light exposures relates to demand characteristics, i.e. the problem of participants finding out the purpose of the study. Obviously, when testing the effects of two different light conditions, it is impossible to blind the participants and/or researcher as is common in e.g. drug research. Participants may be kept unaware of the hypotheses, but it is not unlikely that participants will form expectations about the purpose and hypotheses based on the light conditions, hence they may act in other ways (confirming or rejecting the hypothesis, behaving socially desirable) than if they were blinded [273].

It has been noted that a general challenge with laboratory shift work studies relates to the relatively small number of participants that can be studied under such conditions [271]. Small samples may lead to studies not having sufficient statistical power to detect differences between conditions, thus the probability of making a Type II error, i.e. accepting the null hypothesis when the null hypothesis is false, may increase [274]. Indeed, it has been noted that many studies investigating alerting effects of light have employed small samples increasing the likelihood of biased results [275]. Thus, it is generally recommended to perform a priori power analysis to select a proper sample size. Souman et al. [275] indicated that for an experiment with two conditions analysed with a paired *t*-test, a sample size of $N = 26$ would be needed to detect a medium effect size (Cohen's $d = 0.5$) with power of 0.80 and a significance level of .05. However, in repeated measures designs, even smaller sample sizes may be sufficient, depending on the number of multiple measurements on each participant

within each condition. It is recommended to also pre-register the study protocol and analysis plan [274], to clarify if analyses are exploratory or confirmatory, and as such reduce data mining and selective reporting.

In night work and SD experiments a wide range of measurements methods have been employed, and large variations regarding in research designs and methodology makes comparison between studies somewhat complicated. For instance, field studies of night work often differ in terms of workplace settings, work-schedules, and participant characteristics, hence comparison between studies is often difficult. In terms of the study of human biological rhythms, there has been suggested criteria for matters that needs to be accounted for in the methods [276]. Some of the included criteria that should be reported and/or attended to are; participants' sleep-wake pattern; the season research is conducted; use of tobacco, caffeine and alcohol; ensure that subjects have not undertaken trans meridian travel or night work preceding the experiment; and it is further advisable to assess objective markers of subjects' circadian rhythms. It was also noted that shift work studies should carefully account for and define the working time arrangements and work tasks of employees/participants [276]. An additional challenge in light studies concerns how the light conditions are reported [275], and how to interpret light conditions for comparison between studies. Recent recommendations are to make the whole spectral distribution available, and to report light intensity weighted by the sensitivity of the different photoreceptors [215, 216]. Furthermore, an issue with light studies is that light history may vary among participants, which is known to affect the responses to a light intervention [237].

Both subjective, behavioural, and physiological measures such as subjective sleepiness scales, cognitive performance tasks, and/or EEG recordings, are common in night work and SD studies. Often a combination of multiple measures is preferable, to increase the confidence of results, and/or to detect and investigate differences between measures. In night work and SD research some measures are common and have been validated as reliable and sensitive measures, e.g. the KSS for assessing subjective sleepiness [128], and the PVT for assessing vigilant attention [150]. In terms of

cognitive performance assessment in SD research, a wide range of tests have been employed in addition to the PVT [134, 135]. A challenge with cognitive performance testing is that cognitive performance is not a unitary concept but rely on multiple processes that may be differentially affected by SD [277]. Especially complex tests are haunted by the task impurity problem, i.e. it is difficult to decompose and specify exactly which cognitive processes/faculties that are measured [277]. Furthermore, it is often desirable to repeat cognitive tests to assess the temporal dynamics of performance, e.g. during the night shift. However, practice effects have been noted as the largest problem with repeated testing [135], and complex tests are particularly vulnerable to such effects. Thus, it is common to employ simple test such as the PVT, with minimal task impurity issues, and basically no aptitude and practice effects [278]. On the other hand, the ecological validity of simple laboratory tests may be limited, as simple tests may not predict the very complex tasks one typically encounters in real-life situations [279].

2. Main aims of this thesis

This thesis aimed to investigate how aspects of the physical work environment, in terms of light conditions, can be arranged to facilitate adaptation to night work on measures of alertness, performance, and circadian rhythm. As night work have adverse impact on alertness, performance, safety, and health, it is important to take measures for minimizing such consequences of night work. With the development of LED technology, new opportunities for illumination of workplaces have emerged. To examine the effects of naturalistic LED lighting, a laboratory with standard ceiling mounted tuneable LED-luminaires have been established at the Faculty of Psychology, University of Bergen, Norway (see **Figure 5**). Using these laboratory facilities, three experimental night work studies examined the effects of different light conditions during simulated night work.

Figure 5. The laboratory and participants during a simulated night shift.

Objectives of paper 1

The main aims of paper 1 was to investigate how a full-spectrum (4000 K) bright light (~ 900 lx), compared to a standard light (~ 90 lx), affected alertness and performance during three consecutive simulated night shifts, and timing of the

circadian rhythm after the night shifts. Daytime sleep after the night shifts was also assessed.

It was hypothesized that bright light, compared to standard light, would facilitate alertness and performance during the night shifts, and phase delay the circadian rhythm.

Objectives of paper 2

The main aim of paper 2 was to investigate how monochromatic blue light (λ_{max} = 455 nm), compared to red light (λ_{max} = 625 nm) using similar photon density (~ 2.8 x 10^{14} photons/cm^2/s) across conditions, affected alertness and task performance during a simulated night shift, as well as circadian phase shift following the night shift. In addition, the participants' subjective evaluation of the light conditions, and visual comfort during the night shift was assessed.

It was hypothesized that blue light, compared to red light, would lead to better alertness, mood and performance during the shift, and a larger phase delay of the circadian rhythm.

Objectives of paper 3

The main aim of paper 3 was to investigate how a standard polychromatic blue-enriched white light (7000 K; ~ 200 lx), compared to warm white light (2500 K) of similar photon density (~ 1.6 x 10^{14} photons/cm^2/s), affected alertness and performance during three consecutive simulated night shifts, as well as circadian adaptation to the night work schedule. Additionally, daytime sleep after the night shifts, and participants' subjective evaluation of the light conditions were investigated.

The hypotheses were that 7000 K light, compared to 2500 K light, would increase alertness and performance during the night shifts, and lead to a larger phase delay of the circadian rhythm.

3. Methods

3.1 Procedures

This thesis is based on three experimental studies with separate samples. All three studies employed similar design and procedures, and the study protocol was pre-registered at www.ClinicalTrials.gov, identifier NCT03203538. Each experiment used a counterbalanced crossover study design with repeated measurements. Thus, in each experiment, participants performed two study periods with simulated night shifts, one study period in each light condition. The study periods were separated by a 4-week washout period, and the counterbalanced crossover design entailed that about half of the participants started the trial with the opposite light condition as the other half. In each experiment participants were placed in one of 4–6 groups (maximum nine participants in each group). The first group started with one light condition (e.g. bright light), the second group started with the opposite light condition (e.g. standard light), and similarly for group 3 and 4, respectively. The experiments were commenced in the weekends, and completion of the experiment for four groups took at least eight weeks. Participants were allocated to the groups based on their availability for participation at the specific dates for the two study weekends, and the vacancy in the groups. Hence, participants were sampled into the groups by convenience, though individual participants' order of conditions was random per se.

The counterbalancing and 4-week washout period ensured minimal crossover effects, yet the within-subjects design controlled for interindividual differences. In study 1 and 3, each study period consisted of three consecutive simulated night shifts (i.e. six shifts in total), while in study 2, the participants performed one simulated night shift in each condition (i.e. two shifts in total). The night shifts started at 23:00 hrs, and ended at 07:00 hrs in study 1, and at 06:45 hrs in study 2 and 3. Participants were restricted to the laboratory only during the simulated night shifts, while they slept at home and were largely free to engage in other activities during their spare time. Thus, the studies were semi-controlled naturalistic trials, simulating real-life night work.

Both study periods started three days prior to the first night shift with monitoring of participants' sleep, using actigraphy and sleep diaries, to assess napping behaviour, and to verify that the participants did not significantly shift their circadian rhythm before the simulated night shifts. In paper 1 and 3, daytime sleep after the night shifts was also assessed. In the evening on the day before the first night shift, participants collected saliva samples, at home, for estimation of DLMO before the night shifts (baseline). This procedure was repeated in the evening on the first day following the night shifts to estimate the final DLMO. During the night shifts, five main test bouts comprising the main outcome measures: Positive And Negative Affect Schedule (PANAS) (reported in paper 2 only), KSS, PVT, and a Digit Symbol Substitution Test (DSST) were completed at 23:30, 01:00, 02:30, 04:00, and 05:30 hrs. One test bout took around 20 min to complete. Between main test bouts, participants completed other questionnaires and tests, and had breaks allowing quiet activities. A standardized snack/meal (~ 200 kcal) was provided at about 02:00 and 05:00 hrs, and water was available *ad libitum.* A researcher was present throughout the night shifts to ensure adherence.

3.2 Participants and samples

In all three studies the participants were mainly recruited among students at the University of Bergen via a learning platform, mass e-mail and flyers. The studies used an online survey tool, for screening purposes, before inviting eligible subjects to an enrolment session at the laboratory. Eligible subjects were young adults (between 18-30 years) with good health, and with no current or recent history of diseases/disorders (including psychiatric-, neurological-, and sleep disorders), not on medication (except contraceptives), with normal vision and no colour deficiencies, and who were not pregnant or breastfeeding. Eligible subjects also had to report habitual sleep duration of 6–10 hrs, and wake times between 06:00 and 10:00 hrs, not engaged in night work and/or trans meridian travels in the months prior to or during the study. Extreme chronotypes according to the short Morningness-Eveningness Questionnaire (MEQ) [280], were not included.

In the beginning of the enrolment session thorough information about the study and its purpose was provided, and participants gave their written consent to participate in the study. Participants completed a set of questionnaires including the General Health Questionnaire-12 [281], Dispositional Resilience Scale 15 [282], NEO Five Factor Inventory [283], Bergen Insomnia Scale [284], Global Sleep Assessment Questionnaire [285], Circadian Type Inventory [189], MEQ [286], Munich Chronotype Questionnaire [59]. A practice session of the performance tasks used in the experiments was also commenced during the enrolment session.

Samples

In study 1, 36 participants completed the enrolment session. Four withdrew before the first night shift, four after the first night shift and two prior to the second study period. Two participants were excluded due to non-compliance with the sleep criteria. One got ill and could not attend the last night shift. The data used in paper 1 were from 27 participants, 20 females and 7 males, with a mean age of 21.4 (SD = 2.1) years. Included participants completed at least one of the study periods, and 24 participants completed all the night shifts (i.e. both study periods).

In study 2, the sample consisted of 34 participants completing at least one shift, 27 females and 7 males, with a mean age of 21.6 (SD = 2.0) years. Six participants dropped out after the first night shift, and the second night shift was cancelled for two participants. Paper 2 included data from 31 and 29 participants for the night shift in blue and red light, respectively. Twenty-six completed both shifts.

In study 3, a total of 33 participants completed the enrolment session, two withdrew before the first night shift and one was excluded due to non-compliance with the sleep criteria. Thus, the data in paper 3 were from 30 participants completing at least one study period, 20 females and 10 males, with a mean age of 23.3 (SD = 2.9) years. Data were included from 29 and 28 participants for the night shifts in 7000 K and 2500 K, respectively. Twenty-seven participants completed all the night shifts.

A sample size of 26, required for a paired t-test, has been recommended in studies investigating alerting effects of light [275], although with repeated

measurements designs lower sample sizes may be feasible. As such, using the G*Power 3 software [287], a priori power analysis was conducted. Expecting a medium effect size (Cohen's $d = 0.5$), with significance level set to .05, power at 0.80, and correlation among repeated measurements ($N = 5$) to 0.5 in a repeated-measures within factors design (analysis of variance), 21 participants were calculated to be needed. Changing the number of repeated measurements to $N = 4$, or $N = 3$, yielded that 24 or 28 participants were needed, respectively. The aim was to include 28 participants in each study. However, due to exclusions and drop-outs, complete data were collected for 24, 26, and 27 participants in study 1, 2, and 3, respectively.

3.3 Laboratory and light conditions

The laboratory (30 m^2 room with no windows) was equipped with 20 standard ceiling mounted LED-luminaires (size: 60 x 60 cm), providing uniform illumination without producing glare. These LED-luminaires (Modul R 600 LED CCT/RGB MP; Glamox Luxo Lighting AB, Sweden) can be tuned to provide a range of different light conditions, both in terms of intensity, colour temperature, and monochromatic light. The room had nine available workplaces, separated by partition walls, with similar desktop computers and two LED-luminaires situated above each workplace. Noise cancelling headsets (BOSE QuietComfort 25; BOSE Corp., US) were used during performance testing, and the computer screens were fitted with a filter foil (Metolight SFG-10; Asmetec, Germany) blocking all wavelengths < 520 nm.

Light conditions

Light conditions were measured in the direction of gaze (vertical plane, 120 cm height) at the workplaces using a calibrated spectroradiometer (GL Spectics 1.0 T Flicker; GL Optic, Poland). For paper 1 and 3, light conditions were estimated based on measurements at each workplace prior to the night shifts. In paper 2, light conditions were measured at two workplaces (one in each side of the room) in the beginning, middle, and end of the night shift. The toolbox provided by Lucas et al. [216] was used to calculate the photometric information for the main light parameters seen in **Table 1**.

Table 1. Main light parameters (380–780 nm inclusive). Given as mean (*SD*).

	Photopic illuminance (lx)	Irradiance ($\mu W/cm^2$)	Melanopsin (a-opic lx)	Photon density (photons/cm^2/s)
Study 1 [a]				
Bright light	911 (62)	269 (17)	635 (36)	7.6×10^{14} (4.9×10^{13})
Standard light	91 (6)	26 (2)	57 (11)	7.3×10^{13} (4.8×10^{12})
Study 2				
Blue light	61 (4)	125 (6)	645 (25)	2.9×10^{14} (1.5×10^{13})
Red light	196 (11)	82 (5)	4 (2)	2.6×10^{14} (1.7×10^{13})
Study 3				
7000 K light	197 (19)	61 (6)	192 (19)	1.7×10^{14} (1.6×10^{13})
2500 K light	206 (18)	55 (5)	86 (8)	1.6×10^{14} (1.4×10^{13})

[a] After 05:00 hrs the mean photopic illuminance was 193 lx in both light conditions.

In study 1 a standard colour temperature (4000 K) was used in both light conditions, in study 2 the λ_{max} for the blue and red light was 455 and 625 nm, respectively. The spectral distributions can be seen in **Figure 6**.

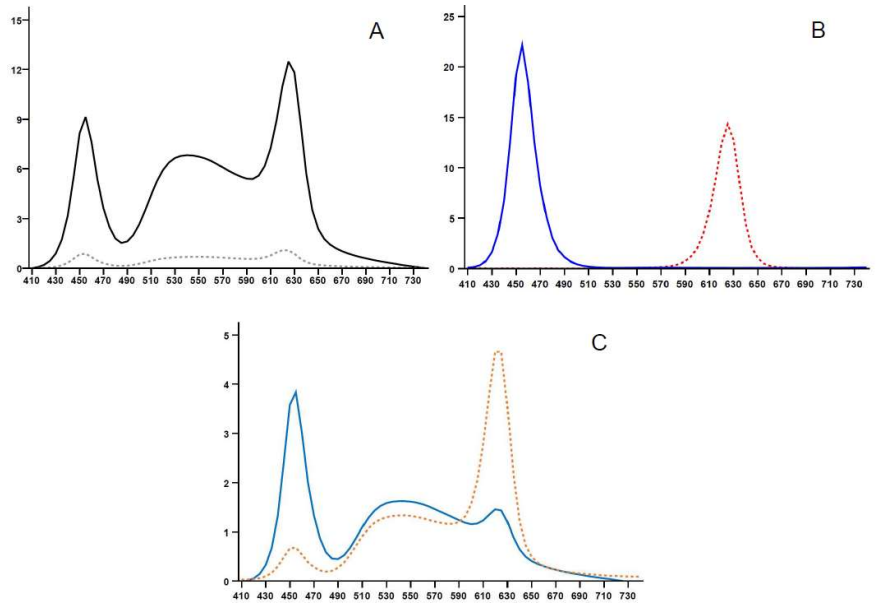

Figure 6. Spectral distributions for the studies. Irradiance ($\mu W/cm^2$/nm) given on the y-axis (the scale differs in A–C), wavelengths (410–730 nm) on the x-axis. **(A)** study 1: black solid line for bright light, grey dashed line for standard light. **(B)** study 2: blue solid line for blue light, red dashed line for red light. **(C)** study 3: blue solid line for 7000 K light, orange dashed line for 2500 K light.

3.4 Measures and instruments

Online screening survey

Several items were used to retrieve relevant information for screening of the participants, such as previous and planned night work and trans meridian travels, self-reported health status, current and previous diseases, use of medication, and habitual sleep times. The short MEQ was used to assess participants' chronotype [280]. Based on questions about preferred rise times and bed times, time of the day with peak performance and self-classification of chronotype, the short MEQ allows for classification of subjects into the following types: Definitely morning type, moderately morning type, neither type, moderately evening type and definitely evening type.

Actigraphy and sleep diaries

Participants' sleep was monitored using wrist-actigraphy (Actiwatch 2 or Actiwatch Spectrum, Phillips Respironics Inc., US) and sleep diaries. Based on the assumption that limb movement is limited during sleep, actigraphy has been validated as a useful tool for measuring sleep [288]. Participants wore the Actiwatch on their non-dominant hand and were instructed to press an event marker when they turned out the lights for sleeping, and when they woke up and started the day. Data were recorded in 1 min epochs in study 1, and 30 s epochs in study 2 and 3. The wake threshold sensitivity was set to medium (40 activity counts per min), and time of inactivity for sleep onset and wake time was set to 10 min (Actiware 6.0, Philips Respironics Inc., US). Usually actigraphy is used in combination with sleep diaries, as the sleep diaries may help to estimate start and end times of the rest intervals. With sleep diaries subjects self-monitor and record their previous sleep episode. Such records can be used to assess metrics such as sleep onset and wake time, sleep onset latency, time in bed and sleep quality [101].

Dim Light Melatonin Onset

Based on the at-home collected saliva samples, the DLMO was estimated before (baseline DLMO) and after (final DLMO) the night shifts. Hourly saliva samples (six samples) were collected at home by the participants, using salivette tubes

(Sarstedt AG & CO, Germany). Baseline sampling started 4 hrs before, and the final sample was collected 1 hr after, participants' habitual bedtime. Final DLMO sampling was delayed by 1 hr relatively to baseline sampling. Participants were provided with dark glasses and instructed to wear them from 1 hr prior to sampling start and during the whole sampling procedure. Additionally, instructions concerning e.g. food, drink, tooth brushing etc. were provided, similar to that reported by Saxvig et al. [289].

Samples were assayed at the laboratory facilities at the Faculty of Psychology, Department for Biological and Medical Psychology, University of Bergen, Norway. Enzyme-linked immunosorbent assay kit (EK-DSM, Bühlman Laboratories, Switzerland), with a detection limit of 0.5 pg/mL, and functional sensitivity of 1.6–20.5 pg/mL was used. Samples were quantified using a Wallac 1420 Multilabel counter (Perkin Elmer Inc., US). DLMO was defined as the time salivary melatonin levels reached 4 pg/mL. Linear interpolation between adjacent samples were used, and if levels reached 3 pg/mL but not 4 pg/mL, linear extrapolation was used. Circadian phase shifts were estimated by calculating the difference between baseline DLMO and final DLMO. In accordance with previous procedures [290], nadir of the CBT was estimated as DLMO + 7 hrs. Based on the final DLMO, and sleep onset and offset (wake time) of the daytime sleep after the third night shift, phase angle after the night shifts was estimated.

Karolinska Sleepiness Scale (KSS)

The KSS comprises a single item assessing the state of sleepiness [123]. Participants indicated their current level of alertness-sleepiness on a 9-point Likert scale with the following steps: 1) very alert, 3) alert, 5) neither alert nor sleepy, 7) sleepy, but no difficulty remaining awake, 9) very sleepy, fighting sleep, strenuous to keep awake. The intermediate steps (2, 4, 6, 8) could also be used, but had no descriptive label.

Psychomotor Vigilance Task (PVT)

The PVT is a simple neurobehavioral task that measures vigilant attention by recording RTs to stimuli occurring at random inter-stimulus intervals [143, 151]. The

PVT is suitable for repeated administration and is nowadays considered the gold standard for detecting neurobehavioral effects of sleep loss and circadian misalignment [278]. All three experiments used a computerized 10-min PVT with similar design/setup as recommended by Basner et al. [150]. Participants were instructed to respond with their dominant hand by pressing the space bar as soon as a stimulus appeared on the screen (see **Figure 7**).

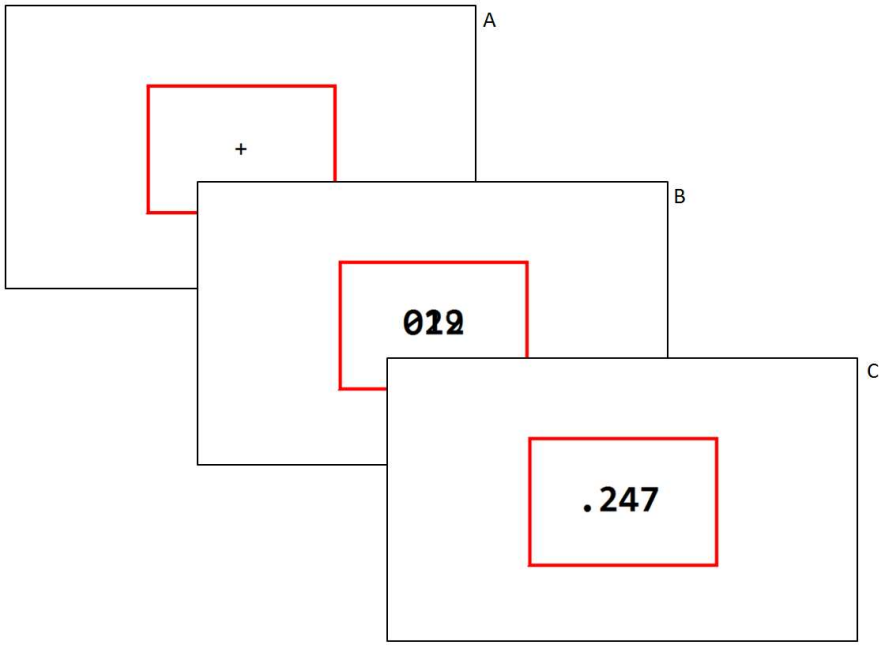

Figure 2. Screen images (example) during one trial of the psychomotor vigilance task. **(A)** No stimulus (1-9 sec). **(B)** Stimulus (counting timer [max 30 sec]). **(C)** RT feedback (1 sec).

All three papers assessed the two main outcome metrics, the mean 1/RT (reciprocal RTs) and the number of PVT lapses (i.e. RTs ≥ 500 ms), as suggested by Basner et al. [150]. In paper 2 the mean RT500 (mean RTs excluding lapses) was also analysed, while in paper 3 the number of false starts (responses without a stimulus), the fastest 10% RT (mean RT of the 10% fastest RTs) and the slowest 10% 1/RT (mean 1/RT of the 10% slowest RTs) were analysed in addition to the aforementioned main outcome metrics.

Digit Symbol Substitution Test (DSST)

Digit symbol substitution tests are assumed to measure complex attention [291], and the DSST is considered a sensitive measure for detecting change in cognitive function [292]. However, the DSST has low specificity in terms of determining which cognitive domain that has been affected [292]. A computerized version was used in all three experiments. Participants were instructed to pair nine target symbols, randomly and individually presented at the centre of the screen, with their corresponding digit in a symbol-digit array shown at the bottom of the screen (see **Figure 8**).

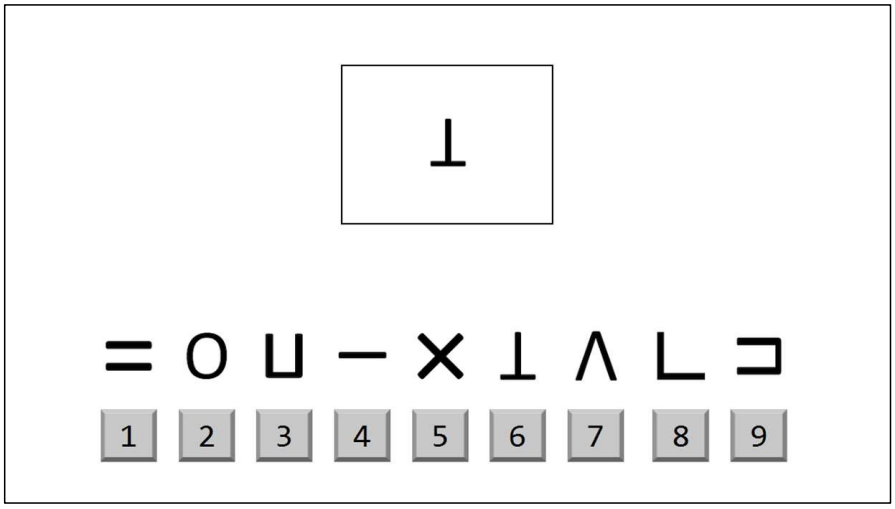

Figure 8. Screen image (example) during the digit symbol substitution test.

The response was given using the mouse pointer, and if no response was recorded after 5 s, the next trial began. In study 1 the test duration was 90 s, while in study 2 and 3 a test duration of 120 s was used. The symbol-digit pairs were randomized for each administration of the test. The outcome measure from the DSST was the number of correct responses during the test.

Other measures

In addition to the measures described above, the 17-plate Ishihara Test for Colour Deficiency was used to ensuring that participants had normal colour vision. In paper 2 and 3, subjective evaluation of the lighting was assessed using a questionnaire

with nine items rated on a 7-point semantic differential scale, adopted from Smolders et al. [293, 294]. The first four items assessed the pleasantness of the lighting: 1) unpleasant-pleasant, 2) uncomfortable-comfortable, 3) disturbing-not disturbing, 4) causing glare-not causing glare. The pleasantness subscale showed internal reliability with Cronbach's α of .87 and .82 in study 2 and 3, respectively. Single items were used to assess the clearness (unclear-clear), colour (warm-cold), brightness (dim-bright), if the light was activating (relaxing-stimulating), and if the light was suitable for work (unsuitable-suitable). In paper 2, PANAS was used to measure mood. The PANAS assesses two factors of mood, positive and negative, and comprises 20 items/words that describe different feelings and emotions [295]. For each of the PANAS items participants indicated to what extent they felt a certain way right now, on a 5-point Likert scale ranging from 1) very slightly or not at all, to 5) extremely. The positive and negative mood subscales showed internal reliability with Cronbach's α of .92 and .68, respectively. Paper 2 also assessed visual comfort during the night shifts, using the headache and eye strain scale [296]. This scale comprises 8 items/symptoms: 1) irritability, 2) headache, 3) eye strain, 4) eye discomfort, 5) eye fatigue, 6) difficulty focusing, 7) difficulty concentrating, 8) blurred vision. Participants indicated the degree of symptoms on a 4-point scale (1 = absent, 2 = slight, 3 = moderate, 4 = severe). In paper 3, the menstrual phase (follicular, luteal) of female participants were estimated, based on self-reported last menses onset and usual menstrual cycle length, similar to previously reported procedures [181].

3.5 Statistical analysis

In all papers, the main analyses were conducted using linear mixed model (LMM) and generalized linear mixed model (GLMM) analysis. GLMMs with a negative binominal distribution were used for analysing the PVT lapses, and false starts, as these count variables were skewed towards zero and showed overdispersion. *Light* (condition 1 vs. condition 2), *shift* (night 1, night 2, and night 3), *time* (23:30, 01:00, 02:30, 04:00, and 05:30 hrs), and their interactions (*light*shift, light*time, shift*time, light*shift*time*) were treated as fixed factors. In paper 2, there were no

shift factor included. In all models, *participant* was included as a random factor. In all papers the phase shift magnitude of the melatonin rhythm (DLMO) was also analysed using LMMs with *light* entered as a fixed factor. Multiple comparisons were made using Bonferroni corrections to evaluate differences between light conditions, shifts and time points. For each of the outcome variables, e.g. KSS score and PVT lapses, separate LMMs and GLMMs were conducted. The estimated marginal means and standard errors (*SE*) were reported and/or plotted in the papers to graph the results in the papers. In all papers, the differences in baseline DLMO between light conditions were assessed using paired samples *t*-tests. To investigate if baseline DLMO correlated with the phase shift magnitude, Pearson's product-moment correlation coefficients were calculated. All statistical analyses were conducted using IBM SPSS Statistics, version 25 (IBM Corp., US).

Paper 1

LMMs were modelled for the KSS, PVT mean 1/RT, and DSST, and a GLMM for PVT lapses. Initially, *napping* (nap vs. no nap) was also included as a fixed effect, but there were no significant effects of *napping*, thus the factor was not included in the final models. Paired samples *t*-tests were used to assess differences in daytime sleep, phase angle, and phase shift for participants with complete data.

Paper 2

Three separate LMMs were applied on the PANAS positive mood, negative mood, KSS, PVT mean 1/RT, RT500, and DSST. In a random effect model the random factor *participant* was included. In a main effect model the fixed factor *light* (blue vs. red) was entered. In an interaction effects model the *light*time* interaction was entered. The model fit was compared using a likelihood ratio test, comparing the difference in -2 times the log of the likelihood between the random effect model, main effect model, and interaction effect model, following the chi- square distribution. The degrees of freedom used for comparison equalled the difference in the number of parameters between the compared models. Pseudo R^2 statistics (% explained variance) were calculated based on reduction in variance from the random effects model to the final model. PVT lapses were analysed with a GLMM using a similar modelling

approach as for the LMMs. However, model fit was compared by assessing the Akaike's information criterion and the Schwarz's Bayesian criterion, preferring smaller values. Visual comfort (headache and eye strain symptoms) and evaluation of light conditions were also assessed with LMMs using the approach described above, however the *time* factor for the headache and eye strain symptoms had only three time points (23:15, 03:15, and 06:15 hrs), while for light evaluation there was no time factor (nor interaction) included in the LMM.

Paper 3

As for paper 2, three separate LMMs were applied on KSS, PVT mean 1/RT, fastest 10% RT, slowest 10% 1/RT, and DSST. The modelling approach was similar as described for paper 2, with a random-, main-, and interaction effects model. Likelihood ratio tests were calculated to compare model fit. If there were significant interaction effects despite the likelihood ratio test indicating poorer model fit, the interaction effects models were trimmed (by removing non-significant interactions), before a second likelihood ratio test was conducted. Accordingly, the models with the best fit were used, and corresponding R^2 statistics were calculated. PVT lapses and false starts were analysed using GLMMs in a similar manner as described for paper 2, also including the *shift* factor. Daytime sleep was analysed with LMMs using similar procedures as described for the other measures. *Participant* was included as a random effect, and the fixed factors *light*, *shift*, and the *light*shift* interaction were entered. In paper 3, the light evaluation was analysed with LMMs including *participant* as a random effect, and the fixed factors *light*, *time* (start of first shift vs. end of last shift), and the *light*time* interaction. For participants with complete data, paired samples *t*-tests were used to assess differences in baseline sleep, daytime sleep, phase shift and phase angle.

3.6 Ethical considerations

The studies were approved by the Regional Committee for Medical and Health Research Ethics, health region West, Norway (No. 2016/1903). When enrolled in the study, each participant was given a unique id-number that was used throughout the

study to ensure that data were non-identifiable. A coding key, which could be used to identify participants, was kept separate from the data. It was necessary to be able to identify participants during the study periods, for organizing the trials and for follow-up when they had enquiries during the ongoing study. All subjects gave their written informed consent to participate and could opt out from the study at any time.

The simulated night shifts entailed work hours similar to that employed in real-life shift work and complied with the regulations of working time according to the Norwegian Working Environment Act. As such, the trials were not considered to pose excess risk for participants, other than what is already generally accepted. However, general sleep hygiene advice was given to the participants, and they were also advised not to drive a car during commute home after the night shifts.

In terms of light exposure, the commercially available LED-luminaires were CE-marked and confirms with the European Standard (EN 62471:2008) for photobiological safety [297]. The light conditions in study 1 and 3 were similar to real-life lighting, except that the bright light condition applied moderately high light intensity compared to common real-life lighting. However, the bright light condition still had much lower light intensity than employed in many previous studies. In study 2, the monochromatic light conditions, in particular the blue light, were very different from real-life lighting, hence only one night shift in each light condition was commenced.

Participants were exposed to strenuous work hours in the studies and were compensated financially for their participation. Participants completing study 1 or 3 received 4000 NOK (VISA gift cards), and participants completing study 2 received 1500 NOK (cash). 10 NOK ~ 1 €.

4. Results

4.1 Summary of findings

Paper 1

The results from the analyses of KSS and task performance (PVT and DSST) supported the hypotheses, as bright light (900 lx), compared to standard light (90 lx), significantly reduced sleepiness and performance deterioration during three consecutive night shifts. The KSS scores increased during the night shifts, starting with KSS scores around 4–5, in both light conditions. However, on night 2 and 3, the KSS scores were reduced with bright light at 04:00 and 05:30 hrs. With bright light the KSS scores on night 2 and 3 were around 6–7 at the end of the shifts, while with standard light the KSS scores were around 8. Performance deterioration on the PVT and DSST was reduced with bright light relatively to standard light already on night 1. Performance in terms of PVT RTs (mean 1/RT), PVT lapses, and DSST responses, was significantly better with bright light in the later parts of the shifts. For PVT lapses, the number of lapses increased to around 16 during all night shifts with standard light. With bright light, on night 2 and 3, the number of PVT lapses increased to around 8, i.e. half of that with standard light. For the subset of participants with valid DLMO measures, the melatonin rhythm after the night shifts was phase delayed with an estimated mean of 3:17 (*SE* = 0:23) hrs, and 2:06 (*SE* = 0:15) hrs with bright and standard light, respectively. There was no significant difference in baseline DLMO between light conditions, nor significant correlation between baseline DLMO and the phase shift magnitude. Thus, the results indicated that bright light induced a larger circadian phase delay than standard light. Hence, the hypothesis was supported. Furthermore, daytime sleep duration (actigraphy) was significantly longer after the night shifts with bright light (mean = 6:44 hrs, *SE* = 0:13 hrs) compared to standard light (mean = 6:21 hrs, *SE* = 0:09 hrs). Overall, the results suggest that the bright light intervention was beneficial for participant's sleepiness and task performance during the night shifts and indicate that circadian adaptation and daytime sleep was improved after night shifts with bright light.

Paper 2

One night shift with monochromatic blue light (λ_{max} = 455 nm), compared to red light (λ_{max} = 625 nm) using similar photon density (~ 2.8 x 10^{14} photons/cm^2/s), reduced subjective sleepiness and improved task performance, in line with the hypotheses. There was no beneficial effect of blue light on the measures of mood. Sleepiness was reduced with blue light, compared to red light, from 02:30 hrs onwards. With both light conditions the KSS scores were around 5 in the beginning of the night shift. With blue light the KSS scores reached levels around 7 at 04:00 and 05:30 hrs, while with red light the KSS scores reached levels around 8. PVT mean 1/RT was improved at 02:30 hrs, while PVT RT500 was improved also at 04:00 hrs. With blue light, from 02:30 hrs onwards, the number of PVT lapses was about half of that with red light. At 04:00 and 05:30 hrs, the number of PVT lapses were around 8 and 16 with blue and red light, respectively. For the DSST, there was a main effect of light, indicating improved performance with blue light, although the light by time interaction was not statistically significant. In terms of circadian rhythm, there was a larger phase delay of the melatonin rhythm after the night shift with blue light, compared to red light, with an estimated mean of 1:26 (*SE* = 0:16) hrs, and 0:36 (*SE* = 0:15) hrs, respectively. Thus, the hypothesis of larger phase delay with blue light was supported. There was no significant difference in baseline DLMO between light conditions, nor significant correlation between baseline DLMO and the phase shift magnitude. Participants' report of visual comfort was higher with blue light compared to red light, and there was a statistically significant light by time interaction effect for eye discomfort and eye fatigue, indicating beneficial effects of blue light in the middle and later parts of the night shift. However, with both light conditions visual comfort was reduced during the night shift. The evaluation of the lighting indicated that blue light was evaluated as colder, brighter, and more activating than red light. For the other light evaluation items, no differences between light conditions were found. In sum, the results indicate that the blue light was beneficial, compared to the red light, on measures of nocturnal sleepiness and performance, as well as circadian adaptation.

Paper 3

In paper 3 we found that polychromatic blue-enriched light (7000 K), compared to warm light (2500 K), improved task performance, but not subjective sleepiness during three consecutive simulated night shifts. Thus, the hypotheses were partly supported. The KSS scores increased during the night shifts from around 4–5 at 23:30 hrs to 7–8 at 05:30 hrs, and there was a main effect of light, with lower KSS scores with 7000 K light. However, there were no significant interaction effects of light by time, indicating that 7000 K light did not reduce sleepiness relatively more than 2500 K light during the night shifts. PVT performance deteriorated during the night shifts, and for PVT lapses and false starts performance improved with 7000 K light, compared to 2500 K light, in the end of night 1 and 2. On night 1 at 05:30 hrs, the number of PVT lapses was around 16 with 2500 K light, and around 8 with 7000 K light. Also, for the 10% fastest RTs on the PVT there were significant interaction effects of light by time, indicating faster RTs with 7000 K light. The circadian phase was delayed with an estimate of 2:34 (*SE* = 0:14) hrs, and 2:12 (*SE* = 0:14) hrs with 7000 K and 2500 K light, respectively. The difference did not reach statistical significance hence the hypothesis was not supported. There was no significant difference in baseline DLMO between light conditions, nor significant correlation between baseline DLMO and the phase shift magnitude. Due to missing data the results concerning the circadian phase shift magnitude are somewhat inconclusive and should be interpreted with caution. There were no statistically significant differences in the daytime sleep variables, with mean (*SD*) sleep duration of 6:01 (0:57) and 5:43 (0:58) hrs with 7000 K and 2500 K light, respectively. Regarding the evaluation of the lighting, 7000 K light was evaluated as clearer, colder, brighter, more activating, and more suitable for work than 2500 K light. The 2500 K light was evaluated as more pleasant than 7000 K light, still both light conditions were evaluated as rather pleasant. In sum, the 7000 K light, compared to 2500 K light, seems to be beneficial in terms of performance. There were no statistically significant differences between the light conditions in terms of reduced sleepiness during the night shifts, nor circadian adaptation after the night shifts.

5. Discussion

Technological development has now made cost-effective LEDs available, and standard ceiling mounted LED-luminaires can now easily be installed and used to administer various light conditions at workplaces. Using such LED lighting in simulated night shift studies, the overall purpose of this thesis was to investigate how different light conditions may facilitate adaptation to night work on measures of alertness, performance, and circadian rhythm. The three papers in the present thesis have documented that sleepiness increases and performance deteriorates during night shifts, and that different LED-based light conditions may reduce such alertness and performance deficits. The results also indicate that the circadian rhythm and daytime sleep may be differentially affected by the employed light conditions. The most important findings of this thesis are summarized in the following:

1. During simulated night work, subjective sleepiness increases, and task performance is reduced, probably due to circadian misalignment and increased homeostatic sleep pressure.
2. Bright full-spectrum (4000 K) light (900 lx) compared to a standard light (90 lx), administered from 23:00 hrs until 05:00 hrs, reduces sleepiness and performance deterioration during three consecutive simulated night shifts.
3. Monochromatic blue light (λ_{max} = 455 nm), compared to photon matched (~ 2.8 x 10^{14} photons/cm^2/s) red light (λ_{max} = 625 nm), reduces sleepiness and performance deterioration during one simulated night shift.
4. Blue-enriched white light (7000 K; ~ 200 lx), compared to warm white light (2500 K) using similar photon density (~ 1.6 x 10^{14} photons/cm^2/s), reduces performance deterioration, but not subjective sleepiness during three consecutive simulated night shifts.
5. Light exposure during simulated night work, affects the amount of circadian phase shift following the night shifts. Especially, bright light (900 lx) compared to standard light (90 lx), and monochromatic blue light compared to red light, seems to phase delay the circadian rhythm.

5.1 Sleepiness and reduced performance during night work

Previous studies have reported increased sleepiness and reduced performance during night shifts, both in real-life and simulated night work studies [6, 27, 41]. The findings in all the papers included in this thesis are in line with these previous reported results. The initial KSS score at 23:30 hrs on the first night shift was around 5 in all three studies and increased to around 7–8 at 05:30 hrs, depending on light condition. These numbers are slightly higher than reported in the real-life studies of nurses and intensive care workers [6, 27], where mean sleepiness (KSS) levels increased from around 4 to near 7, during the first night shift. The higher sleepiness reported in the present studies, is likely due to night shifts starting two hours later, and that the KSS score is the average of KSS assessments before and after the performance tasks (i.e. PVT and DSST). It is known that such tasks may induce additional sleepiness, hence higher KSS rating [58]. Another explanation to the difference may be that naturalistic studies represent more activating and varied stimulation (e.g. walking and attending a sick patient) compared to more monotonous laboratory-based tasks, which mostly involve sitting in front of a computer. In paper 1 and 3, sleepiness was reduced on night 2 and 3, compared to night 1. Reduced sleepiness with consecutive night shifts has also been reported previously [6, 41]. Such reduced sleepiness is likely due to increased homeostatic sleep pressure during the first night shift compared to subsequent shifts and reduced circadian misalignment on subsequent shifts. Indeed, it has been reported that workers are awake substantially longer in connection with the first night shift than with subsequent shifts [6, 27]. Still, the results are at odds with findings showing that the risk for accidents increases with consecutive night shifts [7].

In all three studies the performance on the PVT and DSST worsened from the start to the end of the first night shift. On the PVT, performance deterioration was found both in terms of a general slowing of RTs and an increase in number of omission (PVT lapses) and commission (false starts) errors, depending on light conditions. These results are also in line with previous findings among night workers [6], and simulated night shift experiments [41]. In contrast to the KSS findings, the results in paper 1 did not reveal improved PVT performance on night 2 and/or 3,

compared to the first night shift. On the other hand, the DSST performance improved on night 3 compared to night 1 in both paper 1 and 3. The DSST is known to show practice effects with repeated administration [292], which may explain the difference from the PVT results in paper 1, as the PVT is known to show minimal practice effects [278]. Discrepancy between KSS and PVT has previously been reported [6]. Limited sleepiness and performance adaptation were reported by McHill et al. [41], while higher number of consecutive night shifts had negative impact on PVT performance in another study [157]. In paper 3, there were indications of improved PVT performance with consecutive night shifts, as there were fewer PVT lapses in the end of the shift on night 3, compared to night 1.

It may be difficult to evaluate the practical implications of slightly slower RTs (e.g. 350 vs. 300 ms). However, the implications of lapses of attention can clearly be related to safety issues, as inattentiveness has the potential to compromise safety in real-life tasks (e.g. driving). As such, PVT lapses has been found to predict variability in lane position during a driving simulator task [298]. Furthermore, PVT performance at blood alcohol concentrations of 0.05% in a rested state (at 22:00 hrs), revealed number of PVT lapses around 6 [299]. The estimated number of PVT lapses increased dramatically during the night shifts, from 0–4 at 23:30 hrs for all light conditions, to numbers around 16 at 05:30 hrs for some of the light conditions.

5.2 The impact of light during night work

Bright light

Bright light can be used to elicit nonvisual responses in humans, e.g. phase shift circadian rhythms as well as acute alerting responses. The principles for bright light eliciting such responses have been used in simulated night shift studies, usually in combination with scheduled darkness, and indicate that bright light has great potential to counteract the immediate negative effects of night work [245, 248, 290, 300]. Although effects are not as clear-cut as in simulation studies with high experimental control, also field studies in different occupational settings have reported beneficial effects of nocturnal (intermittent) bright light exposures [254, 256, 301-305]. The

previous studies have mainly applied specialized lighting set-ups using therapy lamps and light boxes for administration of the bright light. As such, workers must remain in front of the light source to receive bright light exposure, and in real-life workplaces this may not be practical or feasible due to work task requirements. Lowden et al. [256] administered bright light via ceiling mounted luminaires in a designated room where the night workers sojourned during their 20-min breaks. Hence, there is a need for studies investigating how night workers may be affected by more uniformly brightly lit work environments.

The results in paper 1 largely supports previous research findings of alerting and performance enhancing effects of bright light, and suggest that beneficial effects can also be acquired using standard ceiling mounted LED-luminaires for administration of bright light. Paper 1 found that the alerting and performance enhancing effects emerged in the later parts of the night shifts, close to the nadir of the CBT when sleep propensity is high [57], which is a typical finding in studies of nocturnal bright light exposure. In paper 1, no differences in subjective sleepiness levels between conditions were reported on night 1, while task performance was improved already on the first night shift. Discrepancy between bright light effects on KSS and PVT performance has also been reported previously [306]. Such findings suggest that bright light has acute alerting effects, as detected by the performance tasks, while the effect on subjective sleepiness is not evident before night 2 when the homeostatic sleep pressure and circadian misalignment was likely reduced. The finding of improved DSST performance suggests that bright light has the potential to conserve performance also on more complex attention tasks relying on multiple cognitive capacities [292]. This finding contrasts a previous field study [301], reporting no statistically significant difference in DSST performance during night shifts with bright light and night shifts with room light.

Late night work is usually associated with KSS ratings slightly below 7 (sleepy, but no difficulty remaining awake), while with monotonous tasks KSS ratings from 7–9 (critical for safety) is common [58]. KSS ratings 8–9 is associated with sleep intrusions in the waking EEG [123], and dangerous driving [307]. In paper 1, the

results showed that despite the monotonous performance tasks, with bright light, mean KSS scores on night 2 and 3 remained below 7 during the whole shift. However, with standard light, KSS scores were above 7 in the later parts of all shifts.

While the number of PVT lapses was improved already on night 1, the largest differences between light conditions were seen on night 2 and 3. The number of PVT lapses (0–4 at 23:30 hrs) increased to about 8 and 16, in the later parts of night 2 and 3, with bright and standard light, respectively. Among real-life night workers, the number of lapses on a 5-min PVT increased from 0–2 at the start, to around 4 in the end, of consecutive night shifts [6]. Due to the artificial conditions in the laboratory with limited opportunities for compensating efforts, e.g. physical activation and varied stimulation, one might expect that the non-shift workers in study 1 would have more lapses than found among shift workers at a real-life workplace. However, considering the different PVT duration (5 min vs. 10 min), the performance in terms of PVT lapses with bright light in paper 1 seem similar to that reported in real-life [6]. On the other hand, with standard light, the PVT lapses reached similar numbers as seen in a simulated night shift study of non-shift workers, using a constant posture protocol under dim light conditions [41].

In terms of circadian adaptation, the results in paper 1 (note that data were incomplete) implied larger phase delay of the melatonin rhythm after three night shifts with bright light (3:17 hrs), compared to the standard light (2:06 hrs). In addition, the average daytime sleep duration after night shifts with bright light was longer, indicating that sleep occurred at a more favourable circadian phase position. Thus, the findings corroborate previous studies reporting that bright light can be used for circadian adaptation among night workers [245, 290, 300]. The phase shift magnitude was close to the ~ 4-hr phase delay reported in a previous study of three consecutive simulated night shifts [290]. However, the light exposure differed, as Smith et al. [290] employed five 15-min bright light pulses interspersed by 45 min of dim room light, and dark glasses to avoid light exposure during daytime. Although the phase shift magnitude was smaller than with bright light, the ~ 2-hr phase delay with standard light was larger than the ~ 1-hr phase delay reported for participants exposed to three

nights with 50 lx [290]. Thus, the standard light (90 lx) may also be of sufficient intensity to elicit some circadian phase shifting effects. It should be noted that for some participants a portion of the bright light, apparently occurred also in the phase advancing part of the PRC, hence such exposure may have attenuated the circadian adaptation to the night shifts. Among actual night workers, light exposure relative to the PRC has been reported to explain a large portion of individual variability in circadian adaptation to night work [91].

As found in previous studies [88, 89], workers adapting to a night work schedule may encounter problems readapting to a day schedule after the night work period. Paper 1 did not investigate readaptation after the night shifts, but considering the relative moderate phase shift magnitude, it can be expected that readaptation should be less difficult than reported for offshore workers after seven consecutive night shifts [89]. Scheduled darkness, as used in many previous studies, was not employed in the studies in this thesis. However, general sleep hygiene advice, e.g. dark bedroom, was provided, and due to the high latitude and time of year, daylight exposure in the morning was limited. Thus, at other latitudes and/or times of the year, the results may have been different.

It has been suggested that bright light should be used in combination with scheduled sleep in darkness to sufficiently shift the melatonin rhythm [300]. Furthermore, interventions using bright light during simulated night shifts in combination with scheduled evening sleep, to produce circadian phase advance (in contrast to phase delay) have also been reported to improve night shift alertness, performance, and daytime sleep [306, 308]. However, though recommendations in real-life may be given, sleep will occur *ad libitum*, and the majority of night workers go to bed in the morning directly after the shift. It has been suggested that a compromise phase position, delaying nadir of the CBT into the daytime sleep episode, is preferable for night workers [247]. The main aim of the current study was not to change the circadian rhythm per se, but rather to improve performance during the night shifts. Still, only a few of the participants in paper 1 apparently achieved the compromise phase position, although it is likely that most of the participants with

incomplete data also achieved the compromise phase position after the night shifts. The nine participants with complete phase shift estimates had mean DLMO at 24:00 hrs after the night shifts, hence the estimated temperature minimum (DLMO +7 hrs) would be at 07:00 hrs. This implies that the period with highest sleep propensity occurred approximately when participants were commuting home after the night shifts. In real-life, such timing of the nadir of CBT may be considered unfavourable, especially if workers are driving home as this would coincide with their peak level of sleep propensity and as such pose a clear safety risk [307]. On the other hand, with standard light, the estimated temperature minimum was at 06:00 hrs, which is at the end of the night shift, which is a critical time in terms of elevated risk for performance errors and accidents/injuries. Thus, considerations about issues related to the timing of the period with maximum sleep propensity should be taken in real-life settings, to minimize the risk of compromising safety.

In terms of daytime sleep after the night shifts, paper 1 found that with both light conditions the average sleep onset was around 07:30 hrs. Thus, sleep was initiated only about 30 min after the end of the shift, and not about 60 min which has been reported as the most usual interval [5]. This discrepancy is most likely due to most participants living quite close to the laboratory facilities hence the commuting time home was short. The average daytime sleep duration for the three sleep periods following night 1–3 was longer (and wake time later) with bright light (mean = 6:44 hrs) than with standard light (mean = 6:21 hrs). As sleep duration is regulated mainly by the circadian system, it is likely, as noted earlier, that longer sleep duration after night shifts with bright light, reflects sleep occurring at a more favourable circadian time due to circadian adaptation. It is also possible that the increased light intensity during the shifts with bright light may have induced a higher homeostatic sleep response, as found for illuminance levels around 250 lx compared to dim light [113]. With both light conditions the daytime sleep duration was apparently longer than among healthcare workers, where a mean total sleep time of 5.74 hrs between night shifts has recently been reported [6]. One probable explanation for the participants in the present thesis sleeping longer is that they comprise young adults (mean age = 21.4

years), mainly students, who didn't have to attend to domestic duties in the same extent as the older adults (mean age = 33.8 years) studied by Ganesan et al. [6].

Short-wavelength monochromatic light

Nonvisual responses to light exposure rely on ipRGCs that are particularly sensitive to blue light [309]. Using monochromatic (i.e. narrowband) light exposures, it has been shown that several nonvisual responses, e.g. alertness, melatonin suppression, and circadian phase shifting, is sensitive to short-wavelength light [222, 224, 226]. In paper 2, such findings were largely supported also in a simulated night shift study, employing higher light intensity/photon densities than the previous studies. During a night shift (23:00–06:45 hrs) with monochromatic blue light (λ_{max} = 455 nm), subjective alertness and task performance was improved, and the melatonin rhythm was phase delayed, compared to photon matched (2.8 x 10^{14} photons/cm^2/s) red light (λ_{max} = 625 nm). Like the results in paper 1, the effects of light emerged in the middle and later parts of the night shift when sleep propensity is high. As previous studies have employed specialized lighting set-ups and carefully controlled light exposure procedures, the findings in paper 2 suggests that also when using standard ceiling mounted LED-luminaires, and relatively higher photon densities, short-wavelength light elicits greater nonvisual responses than long-wavelength light.

Subjective sleepiness was reduced with blue light compared to red light, and the KSS scores did not reach the safety critical level, 7, before the assessment at 05:30 hrs. In contrast, with red light KSS scores were > 7 already at 02:30 hrs, and > 8 at 04:00 and 05:30 hrs. While a previous study indicated that blue light (λ_{max} = 479 nm) at lower irradiance (5 x 10^{13} photons/cm^2/s) is more effective at enhancing subjective alertness than red light (λ_{max} = 627 nm) [230], paper 2 reported such effects also with higher irradiance. In paper 2, mood (PANAS) was also assessed, and revealed reduced positive mood scores during the night shift but the night shift had only minor impact on negative mood. This is similar to previous findings [310, 311], which also reported that subjective sleepiness and positive mood are associated, suggesting that these share a similar neurobiological pathway. However, in contrast with the KSS findings, paper 2 found no significant differences in positive mood between the light conditions. There

was a higher negative mood score with blue light at 23:30 hrs, but this difference was only found at the initial assessment, hence it was probably related to a negative initial perception (first impression) of the blue light. Plitnick et al. [311] investigated effects of nocturnal 60-min exposure (from about 01:00 to 02:00 hrs) to monochromatic blue and red light relative to dim light, using similar illuminance levels (10 lx and 40 lx) across the light conditions. Thus, the light exposure and duration was quite different from that reported in paper 2, making comparison somewhat obscured. Nevertheless, Plitnick et al. [311] found that KSS and positive mood were basically mirror images of one another, similar to the findings in paper 2. However, it was also indicated by Plitnick et al. [311], that both the red and the blue light reduced sleepiness and increased positive mood in a similar manner, somewhat contrasting the findings of reduced sleepiness with blue light compared to red light in paper 2.

The PVT performance was improved with blue light in a similar pattern as for the KSS. Both improved RTs and reduced number of PVT lapses were evident. With red light, the number of PVT lapses increased to around 16 in the end of the night shift, similar to that seen with standard light in paper 1 during night 2 and 3. However, with blue light the number of PVT lapses were similar to that found for bright light during night 2 and 3 in paper 1, i.e. around 8. Although comparison may be spurious due to different light exposures and procedures, the PVT findings in paper 2 are in line with the previous reports of improved RTs and reduced lapses with monochromatic blue light [226]. Also, in terms of DSST performance there was a general improved performance with blue light similar to the PVT and KSS, although the light by time interaction did not reach statistical significance.

In paper 2 there were relatively large individual differences in the circadian response to working simulated night shifts with monochromatic blue and red light conditions. Apparently, while most participants showed basically no phase shift of the melatonin rhythm after a night shift with red light, some participants acquired a substantial phase delay. With blue light, most participants phase delayed, while a few participants apparently phase advanced their circadian rhythm. The red light condition had limited direct stimulation of the melanopsin photoreceptors (melanopic lx = 4),

hence the circadian entrainment by melanopsin stimulation was minimal. Still, a recent study [312] indicated that melatonin suppression is predicted to occur at melanopic illuminance levels as low as ~ 1.5 melanopic lx, and indirect stimulation of the ipRGCs via the rods and cones is also possible [67]. Importantly, the light exposure was continuous during the whole shift, hence participants may have been exposed to light both in the phase delay and phase advance parts of the PRC. Considering a PRC specific for blue light [313], it seems however that the blue light exposure was mainly in the phase delay part of the PRC. Interindividual variability in the sensitivity and circadian responses to light have been reported previously [238] and other factors than the light exposure may also impact circadian rhythms [60]. It is not unlikely that behaviours we did not thoroughly control might have affected the results, e.g. light exposure outside the laboratory. The timing of sleep is also of importance [300, 308], and other nonphotic stimulus such as exercise, social cues, and meal timing, may induce circadian phase shifts [314]. Thus, it is possible that other factors than light contributed to the observed individual differences. Nevertheless, the general results in paper 2 are in line with previous findings indicating short-wavelength light sensitivity of the circadian system [224].

Paper 2 also found that visual comfort was generally better with blue light, compared to red light, possibly due to greater pupil constriction driven by the ipRGCs [223]. However, symptoms of visual discomfort were much more pronounced, also for the blue light condition in paper 2, than reported during daytime office hours in a previous study [296]. Neither monochromatic blue light nor red light were evaluated as particularly suitable for work, hence the practical use of such lighting should be investigated further.

Polychromatic blue-enriched light

As monochromatic light exposures may not be applicable due to its visual properties, it has been suggested that polychromatic short-wavelength enriched light, i.e. blue-enriched light, has the potential to elicit greater nonvisual responses than light with less short-wavelength energy. For instance, 17000 K light, compared to 4000 K light, induces greater melatonin suppression [228]. Furthermore, exposure to 17000 K

light, compared to 4000 K light, for 6.5 hrs during the biological night, reduced subjective sleepiness, but did not improve PVT performance during light exposure [229]. In another study, moderately blue-enriched light (6500 K; 40 lx) during 2 hrs in the evening, compared to warm light (2500 K; 40 lx), was also found to induce larger melatonin suppression and reduced subjective sleepiness, as well as improved PVT performance [227]. Chellappa et al. [227] employed relatively low light levels and used the same illuminance for both light conditions, while Hanifin et al. [229] employed higher light intensity (i.e. 123 lx and 96 lx in the 4000 K and 17000 K light, respectively), and photon matching ensuring 1.0 x 10^{14} photons/cm^2/s in both light conditions. These latter illuminance levels are more like typical indoor room lighting. Few simulated night shift studies and/or field studies have investigated the use of blue-enriched light during night work. One study [253] found no effects of 17000 K light (89 lx), compared to standard 4000 K light (84 lx), on sleepiness, task performance, as well as EEG correlates of sleepiness, during simulated night shifts among actual night workers. However, if compared relative to circadian phase 17000 K light reduced subjective sleepiness compared to the standard light [253]. A field study [252] of control room workers exposed to 350 lx of 17000 K light, compared to 4000 K and 6500 K light, found beneficial effects of 17000 K light on measures of sleepiness and performance, and melatonin suppression was greater. Although light conditions vary in the previous studies, findings overall suggest beneficial effects of blue-enriched light during night work, although some inconsistency exists.

In paper 3, it was reported minor albeit beneficial effects of 7000 K light, compared to 2500 K light, for some performance measures, but not on subjective sleepiness, nor were there statistically significant differences between conditions regarding phase shifts of the melatonin rhythm. Thus, the findings concur with the somewhat limited consistency in previous studies. The KSS scores with both conditions apparently reached the suggested safety critical level, 7, at 04:00 and/or 05:30 hrs, depending on night number. With 7000 K light, there was evidence of fewer PVT errors in the later parts of night 1 and 2, as well as faster RTs in the optimal domain of responses in the middle to late parts of the night shifts. Thus, the 7000 K light seems to be beneficial, especially in terms of reduced PVT errors around the time

with highest sleep propensity. The number of PVT lapses on night 1, increased to about 16 at 05:30 hrs with 2500 K light, while with 7000 K light the number of PVT lapses increased to around 8. However, with both 7000 K and 2500 K light, the number of PVT lapses on night 3 was very similar to that seen for the bright light condition in paper 1 on night 2 and 3. Thus, using blue-enriched light seem to be beneficial for PVT performance mainly on the first night shifts, while on the third shift there are no differences in terms of PVT lapses. Participants also evaluated the 7000 K light as more activating than 2500 K light, in line with findings during office hours [293]. Overall, the results suggest that blue-enriched light have minor but beneficial effects for night worker's alertness and performance, yet further research is needed to validate these findings and maximize the effectiveness of blue-enriched light.

In terms of circadian phase, with both 7000 K and 2500 K light, the melatonin rhythm was estimated to be delayed, with 2:34 and 2:12 hrs, respectively, not reaching statistically significant difference. For more than half of the participants, in both light conditions, the phase delay was apparently not sufficient to reach the compromise phase position (i.e. nadir of the CBT occurring during the daytime sleep episode). Considering daytime sleep after the night shifts, paper 3 indicated no significant differences between light conditions. Similarly, a study comparing sleep after SD with exposure to 250 lx of 9000 K light, compared to 2800 K light, found no differences in sleep parameters between the light conditions [113]. Paper 3 reported that with both light conditions the average sleep onset was at 07:45 hrs, and the sleep onset latency was around 0:05 hr after the night shifts with both 7000 K and 2500 K light. The short sleep onset latency and initiation of sleep around 1 hr after the end of the night shift, concur with typical sleep patterns for night workers [5]. The average daytime sleep duration was 6:01 and 5:43 hrs with 7000 K and 2500 K light, respectively. This is relatively similar to the total sleep time reported between night shifts among healthcare workers [6].

A factor complicating the evaluation and comparison of studies using blue-enriched light conditions, is the different spectral distributions, and the different light intensities employed. For example, the study by Motamedzadeh et al. [252] compared

light conditions keeping the illuminance level (350 lx) the same across conditions, while Hanifin et al. [229] compared light conditions with different illuminance levels, as the photon densities were equated. As photoreceptors act as photon counters [210], the clear-cut effects reported by Motamedzadeh et al. [252] may hinge on higher photon density in the 17000 K condition rather than differences in wavelengths. Thus, if the photon densities were equated as in the study by Hanifin et al. [229], the results might be different. However, Motamedzadeh et al. [252] investigated lighting at a real-life workplace and ensuring adequate visual qualities (i.e. illuminance) may demand unequal photon densities of light with different spectral distribution. In paper 3, the photon density employed was similar across conditions. Despite substantially higher melanopic illuminance, there were only minor effects of 7000 K light, compared to 2500 K light. One possible explanation for the limited effectiveness of the blue-enriched light, may be use of saturating light levels as also suggested by Sletten et al. [253]. For instance, when using light boxes, bright blue-enriched white light (17000 K) is no more effective than standard bright light (4100 K), with similar photon density (~ 4.2 x 10^{15} photons/cm^2/s), in phase shifting the circadian rhythm [232, 233]. Interestingly, the number of PVT lapses on night 2 and 3 in paper 3 are not very different from the numbers seen on night 2 and 3 with bright light in paper 1. As such, the notion of saturating light levels seems to be a likely explanation for this.

5.3 Limitations and methodological considerations

In general, it is difficult to compare experimental studies of SD, night work, and light exposure. The design and methodology may differ substantially between studies, e.g. with light studies it may be challenging to compare light conditions, as noted in the previous paragraph. As such, there are methodological considerations and some limitations that should be noted with the studies in the present thesis.

Research design

The studies in this thesis were designed as experimental and controlled trials. However, a hybrid solution was used with simulated night shifts in the laboratory, and real-life conditions during spare time outside the laboratory. As such, experimental

control was kept during night work in the laboratory, while the real-life aspects to some degree was maintained as participants were sleeping at home, and were largely free to engage in activities and manage their own spare time. Note that there were restrictions concerning caffein, tobacco, alcohol, and to some extent napping (paper 1 and 3 had restrictions on timing and duration of naps, while paper 2 did not allow naps). Furthermore, participants were required to extend their period of wakefulness by 1 hr during baseline DLMO sampling. Nevertheless, the studies were simulating real-life night work. An advantage with the employed approach is that the studies have ecological validity, in that the design includes the dynamics between work, spare time, and sleep, being somewhat transferrable to a real-life work situation. A drawback with the design is that potential confounders such as light exposure, sleep, and other behaviours outside the laboratory, complicates and likely have distorted the results. In particular, the light history and light exposure of the participants may have affected the results, e.g. differences in light exposure in the morning after the night shifts. However, the experiments were conducted at relatively high latitude and a time of year with limited daylight exposure in the hours before and after the night shifts. Still, it is likely that differences in spare time light exposure and other behaviours occurred, both between and within individuals.

As individual variation in responses to light and SD/night work is known [141, 238], a repeated measures design was employed, hence the results should be minimally affected by inter-individual differences. The order of conditions was counterbalanced, and the study periods were separated by one month, hence order and crossover effects were also controlled. One other concern when designing light studies, relates to demand characteristics, as it is not possible to introduce blinding of the subjects to the light conditions used. For instance, knowledge about the effects of blue light is probably increasing as e.g. blue light filters are becoming standard software applications on cell-phones, computers, and tablets [315]. Thus, it is likely that participants may have developed expectations in terms of study hypothesis. One way to reduce the effects of demand characteristics related to light exposure could be to e.g. administer placebo caffeine pills to all participants, hence reduce the focus on light conditions. However, the studies in this thesis did not employ such strategies.

Participants and samples

The participants were not night workers, and as actual shift workers may cope better with SD in the laboratory than non-shift workers [272], the transferability to real-life night work is somewhat limited. Furthermore, the participants were screened and selected young healthy adults, not representative for a shift working population. However, the selection of participants was made to avoid biases in terms of e.g. extreme chronotypes, age differences, sleep, and health issues, which are all of importance in the study of human biological rhythms [276]. By studying a homogenous sample, the confounding factors may be reduced, thus increasing the internal validity. However, although the participants may be considered a homogenous group, it is still possible that differences in terms of e.g. light sensitivity and tolerance to SD, affected the results. For instance, genotype has been related to both sleepiness and insomnia among shift workers [161, 194], and nonvisual effects of light have also been reported to depend on genotype [241]. Although selected based on chronotype assessed with the short MEQ, there were considerable variation in the baseline DLMO estimates ranging from around 19:00 to 24:00 hrs. As most participants were females, the generalizability to other gender distributions may not be feasible. However, males have been suggested to have larger nonvisual responses to light [240], hence in a more equal gender distribution, the beneficial effects may have been greater than suggested by the studies in this thesis. There were also challenges with dropouts in all studies, and most of the dropouts occurred after the first night shift. Although not documented, many of the dropouts, indicated that it was too demanding to complete all the shifts, and some felt that it would interfere too much with other duties (e.g. studying). This may indicate that vulnerable participants were inclined to dropout, while those coping with the night shift remained and completed the study, i.e. a healthy worker/participant effect may have affected the results. For instance, it has been suggested that especially individuals vulnerable to sleep loss may benefit from light exposure [213, 241].

The studies employed sample sizes based on a priori power analyses. In all three studies the sample size ($N \geq 24$) was higher than in most of the previous studies assessing alerting effects of light [275]. For instance, in the controlled laboratory trials conducted by Czeisler et al. [245] and Lockley et al. [226], a sample size of 8 and 16

was used, respectively. Thus, the likelihood of Type II error, and biased results, due to small sample size may be considered relatively low. On the other hand, this notion hinges also upon the expected effects based on the light conditions used. Within paper 1 and 2, the relative difference between the employed light conditions (e.g. in terms of melanopic lx) were large, hence they may be expected to elicit largely different degrees of nonvisual effects. In paper 3, the relative difference between the employed light conditions (e.g. melanopic lx) were much smaller than in both paper 1 and 2, although very different in terms of colour temperature. Thus, it is possible that paper 3 was underpowered compared to paper 1 and 2, and the likelihood of Type II error may be increased. In all papers the incomplete phase shift estimates increase the risk of biased results in terms of the circadian rhythm measures.

Measures

Most of the instruments and measures used in this thesis are standard measures, frequently used in SD, night work, and light research, and their reliability and validity have been assessed in previous studies. Actigraphy is considered a reasonable valid and reliable instrument for assessing sleep in healthy normal individuals [316]. However, actigraphy is not good at detecting wakefulness within sleep episodes, but in terms of sleep duration and total sleep time, depending on studied population, actigraphy data correlate reasonably well with PSG [100]. To be able to properly estimate the start and end times of rest periods, a standardized sleep diary similar to the consensus sleep diary [101], was used in addition to actigraphy. Both the KSS, PANAS, PVT, and DSST are considered valid and reliable measures, although the DSST is known to show practice effects [292]. Considerations should be taken regarding the real-life relevance of the simple tasks performed under artificial conditions in the laboratory, such as the PVT. In real-life situations much more complex tasks are normally encountered. Such tasks are known to rely on multiple cognitive capacities, and may not be as vulnerable to sleep loss and circadian misalignment as the PVT. On the other hand, the PVT may be repeated with limited practice effects as seen in more complex tasks, hence the PVT is suitable for assessing the temporal dynamics during a night shift. PVT performance have also been

suggested to have ecological validity as it can reflect real world risks [150], in that many applied tasks rely on timely reactions and sustained attention, e.g. driving.

The subjective measures assessing visual comfort and evaluation of the lighting are not that common, and the validity may be questioned. The headache and eye strain scale was used in a previous study [296] of daytime office workers and was shown to be sensitive to exposure of different light conditions. The items assessing evaluation of the lighting were adapted from previous studies finding that evaluation differ with different intensities and spectral distributions of polychromatic light [293, 294].

In terms of the employed measures, a main limitation concerns the circadian phase shift estimates based on the DLMO sampling. That is not due to the methodology per se, as estimation of DLMO is a validated measure of circadian phase [317], also with at home sampling procedures [82]. The problem concerns issues with the employed sampling protocol and possibly participants' adherence. Especially in paper 1, only a small subset (33%) of the participants' circadian phase shift could be estimated after the night shifts with bright light, mainly due to no observed rise in the melatonin concentration during the final sampling period. Apparently the final DLMO shifted to a later time than accounted for in the sampling protocol (i.e. last final DLMO sample 2 hrs after usual bedtime), but also possibly due to light exposure suppressing melatonin, or other adherence issues. In the other light conditions, the sampling protocol seemed to work better, although phase shifts could only be calculated for 61–79% of the participants. This suggests that a constant routine protocol would be preferable for assessment of circadian phase, and/or that the DLMO sampling should have been conducted in the laboratory controlled by a researcher or conducted over a wider time frame. Furthermore, the findings stress the importance of carefully planning the timing of the sampling, and the importance of protocol adherence if sampling at home is employed. Previous studies have also reported challenges with missing DLMO estimates using at home sampling procedures [82, 289].

5.4 Strengths

While there are many factors that might have impacted the results, as participants were mainly free to manage their spare time and sleep, this may also be viewed as an asset in terms of generalizability and ecological validity. The light conditions were administered using standard ceiling mounted LED-luminaires, which can be installed and implemented at a real-life workplace. In that sense the studies have novelty, and a general strength across the studies is that the employed light interventions put minimal requirements on participants for adherence, and administration of light exposure did not interfere with work tasks. Thus, the interventions can easily be transferred to real-life workplaces. Another strength is the repeated measurements crossover design using counterbalancing, which limit the impact of crossover effects and individual differences. Additional strengths of the studies are the use of validated instruments, e.g. KSS and PVT, and repeated administration for assessing the dynamics during the shifts. In addition, the analysis strategy used should be considered a strength as the use of LMM and GLMM allows for missing data without excluding cases completely as with analysis of variance.

In paper 1 and 3, the light conditions employed were suitable for, and somewhat similar to (except the bright light), real-life application. In paper 2 and 3, the light conditions were photon matched, hence we investigated the impact of short-wavelength light compared to long-wavelength light, while controlling for light intensity.

5.5 Ethics

The ethics committee approving the studies only allowed individuals to participate in one of the studies, as the demanding work schedules should not interfere too much with other duties (e.g. students study). Other concerns may relate to the adverse effects of night work and light exposure. The participants were exposed to strenuous work hours, albeit still in compliance with regulations of working time. In a short-term perspective the employed light conditions were not considered to pose any

health risks, however participants did experience some visual discomfort especially with the monochromatic light conditions reported in paper 2. Furthermore, it is likely that some participants encountered some problems readapting to a day schedule after the simulated night shifts. It is also possible that light exposure in rare instances may trigger sleep disturbances, i.e. individuals with delayed sleep wake disorder are particularly sensitive to light exposure [239]. However, participants were screened prior to the study to avoid such problems. In terms of employing similar light conditions at real-life workplaces, some caution should be taken, as there are concerns regarding long-term effects of light at night and prolonged blue light exposure [266, 268]. Another issue worth mentioning is that even though participants were compensated for their efforts, compared to real-life night work, payment was low.

5.6 Conclusions and further direction

This thesis has contributed to the research field by investigating how LED-based lighting can be used to facilitate adaptation to simulated night work. The findings across studies indicate that standard ceiling mounted LED-luminaires can be used to administer different light conditions, with the potential to modulate the impact of working outside standard working hours, i.e. night work. Thus, the use of similar LED lighting should be investigated also in real-life workplaces, with actual night workers. The present studies employed homogenous samples of healthy young adults with a skewed gender distribution, hence replications with other populations (e.g. more males and older workers) need to be conducted. Future studies should also assess other measures, e.g. more complex cognitive tasks, to investigate if the effects of the light conditions are task specific, and if various cognitive capacities may be affected differently. Another important issue to address in future studies is individual differences in responses to nocturnal light exposure and tolerance to night work.

The results of paper 1 suggests that full-spectrum (4000 K) bright light (~ 900 lx), compared to a standard light (~ 90 lx), reduces sleepiness, and improves performance during three consecutive night shifts. Paper 1 also indicated that bright light may hasten circadian adaptation and suggested increased daytime sleep duration

after the night shifts with bright light compared to standard light. As such, these findings have implications for the recommended light intensity that should be employed at real-life workplaces during night work. Increasing the light intensity may have beneficial implications both in terms of safety and productivity, as well as workers' wellbeing with reduced sleepiness and improved sleep. The standard light condition of 90 lx at eye level seems to have too low light intensity for being recommended for night work. The results in paper 2 suggests that monochromatic short-wavelength blue light (λ_{max} = 455 nm), compared to long-wavelength red light (λ_{max} = 625 nm) with similar photon density (~ 2.8 x 10^{14} photons/cm^2/s), reduces sleepiness, and improves performance, and circadian adaptation during one simulated night shift. Paper 2 also indicates that monochromatic light conditions, previously administered with specialized lighting set-ups, can now be provided using standard LED-luminaires. Using such light conditions may not be feasible at a real-life workplace, but the findings warrants more research to assess the applicability at workplaces, as well as for treatment purposes. The results of paper 3 indicated minor, yet beneficial effects during three consecutive night shifts with ~ 200 lx of blue-enriched white light (7000 K), compared to warm white light (2500 K). However, the effects may have important implications as 7000 K light apparently reduces the number of omission and commission errors during a sustained attention task in the early morning hours. Thus, safety may be improved during similar applied task, e.g. driving, or monitoring in a control room, by exposing night workers to blue-enriched light. More research in applied settings is needed to validate these findings.

LED lighting has great potential for eliciting favourable nonvisual effects among night workers, and as such improve adaptation to night work. However, further research is warranted to investigate the applicability at real-life workplaces. There is also a need to address possible adverse effects of nocturnal light exposure, in particular long-term effects. Future research should also explore more light conditions and combinations, e.g. dynamic LED lighting (changing spectral characteristics across the day/night), that can be favourable for night workers, in order to develop recommendations for illumination of night workers workplaces.

6. References

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Article

Alerting and Circadian Effects of Short-Wavelength vs. Long-Wavelength Narrow-Bandwidth Light during a Simulated Night Shift

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Abstract: Light can be used to facilitate alertness, task performance and circadian adaptation during night work. Novel strategies for illumination of workplaces, using ceiling mounted LED-luminaires, allow the use of a range of different light conditions, altering intensity and spectral composition. This study (ClinicalTrials.gov Identifier NCT03203538) investigated the effects of short-wavelength narrow-bandwidth light (λ_{max} = 455 nm) compared to long-wavelength narrow-bandwidth light (λ_{max} = 625 nm), with similar photon density (~2.8×10^{14} photons/cm^2/s) across light conditions, during a simulated night shift (23:00–06:45 h) when conducting cognitive performance tasks. Light conditions were administered by ceiling mounted LED-luminaires. Using a within-subjects repeated measurements study design, a total of 34 healthy young adults (27 females and 7 males; mean age = 21.6 years, SD = 2.0 years) participated. The results revealed significantly reduced sleepiness and improved task performance during the night shift with short-wavelength light compared to long-wavelength light. There was also a larger shift of the melatonin rhythm (phase delay) after working a night shift in short-wavelength light compared to long-wavelength light. Participants' visual comfort was rated as better in the short-wavelength light than the long-wavelength light. Ceiling mounted LED-luminaires may be feasible to use in real workplaces, as these have the potential to provide light conditions that are favorable for alertness and performance among night workers.

Keywords: short-wavelength light; night work; sleepiness; alertness; performance; circadian rhythm

1. Introduction

At the beginning of this century it was established that humans have nonvisual photic input from a subset of intrinsically photosensitive retinal ganglion cells (ipRGCs) expressing the photopigment melanopsin, which is maximally sensitive to short-wavelength light [1–3]. These ipRGCs project directly to the main circadian pacemaker located in the hypothalamic suprachiasmatic nuclei (SCN),

and this pacemaker controls and coordinates circadian rhythms [1,2]. Further insights have revealed that ipRGCs also project to various brain areas involved in sleep–wakefulness regulation, mood and even higher order cognitive processes [4–6]. Although melanopsin is the primary photopigment eliciting nonvisual effects, classical rods and cones also contribute to nonvisual responses to light via input to the ipRGCs [7,8].

Nonvisual responses sensitive to short-wavelength light include suppression of melatonin production [9,10], circadian phase shifting [11,12], pupil responses [13], and enhancement of alertness and performance [14–16]. It has been suggested that the alerting effects of light are strongest at night [5], when the circadian- and homeostatic drives for sleep are high, as postulated by the two-process model of sleep regulation [17]. Accordingly, several previous studies reporting alerting effects of short-wavelength narrow-bandwidth light [14,15,18] were conducted late in the evening or during the biological night, under relatively high circadian- and homeostatic sleep pressure. During the night, the alerting effects of short-wavelength light are induced by counteracting both the circadian and homeostatic drives for sleep, while during the day only the homeostatic sleep pressure is affected [19].

Especially at lower light intensity levels, short-wavelength narrow-bandwidth light (λ_{max} = 479 nm) was found to be more effective for eliciting subjective alerting responses than long-wavelength narrow-bandwidth light (λ_{max} = 627 nm), while at higher intensity levels the difference becomes less clear [20]. Note that long-wavelength narrow-bandwidth light (λ_{max} = 630 nm) also seems to be able to enhance alertness and performance compared to dark conditions [21,22]. Such findings have also been reported during daytime, as long-wavelength light improved alertness, assessed with electroencephalography, relative to darkness [23]. It was further noted that melatonin suppression is thus not needed for eliciting alerting effects in humans. Common for the previous narrow-bandwidth light studies were strict control of light exposure, and administration by special lighting set-ups such as custom-made light spheres [9–11,14,19,20], light goggles [15,21], light visors [16], or light boxes [22]. While the use of such specialized lighting set-ups allows for well controlled laboratory trials, the suitability in real-life settings may be limited.

Night work has consistently been associated with alertness and performance deterioration [24,25], and light interventions have the potential to counter these immediate effects of night work, both by its acute alerting properties [26] and via circadian phase shifting [27]. However, reviews of interventions to reduce the negative impact of night work (also chronic health effects) have indicated that definite conclusions on the beneficial effects of light interventions during night work cannot yet be drawn [28,29]. Recently, it was also noted that although most field studies indicate some beneficial effect of light during night work, methodological issues and diversity preclude conclusion about appropriate light schedules for night shift workers [30].

Due to nonvisual responses being sensitive to short-wavelength light, there has been an interest in employing short-wavelength enriched (i.e., blue-enriched) white light as a countermeasure against some of the negative impacts of night shift work. As such, recent studies have suggested beneficial effects of blue-enriched light on nocturnal alertness and performance [31–33]. On the other hand, an issue with the use of light interventions during night work, especially short-wavelength light, is the potential negative effects associated with light at night, e.g., melatonin suppression has been suggested as a mechanism for the increased risk of cancer among night shift workers [34,35]. Thus, studies have also investigated short-wavelength depleted/attenuated white light during simulated night shifts [36–38]. These studies have indicated that such lighting can reduce melatonin suppression and phase shifting of the melatonin rhythm, without having a negative impact on alertness and performance.

The development of light emitting diodes (LED) has made light characteristics such as spectral composition and light intensity easily controllable [39]. Thus, light exposures previously administered by specialized lighting set-ups, can now be administered via standard ceiling mounted LED-luminaires applicable for illumination of workplaces. However, only a few recent studies have used such LED-based lighting during simulated night work [33,40,41]. The effects of narrow-bandwidth lighting using ceiling mounted LED-luminaires during night work have not yet been investigated.

Most previous studies reporting alerting effects of short-wavelength narrow-bandwidth light have employed relatively low photon density [14,15,18,19], hence there is a lack of studies investigating narrow-bandwidth light levels that could be sufficient for a workplace setting. Three previous studies [14,15,19] used photon matching and a photon density of 2.8×10^{13} photons/cm^2/s, comparing short-wavelength narrow-bandwidth light (λ_{max} = 460 nm) and medium-wavelength narrow-bandwidth light (λ_{max} = 550–555 nm) light. One study [18] compared short-wavelength narrow-bandwidth light (λ_{max} = 460 nm) and long-wavelength narrow-bandwidth light (λ_{max} = 640 nm), using an even lower photon density of 5×10^{12} photons/cm^2/s (~1.0 lx). The latter study, however, was targeted towards work situations such as driving, where low intensity light would be practical.

The aim of the current study was to investigate how short-wavelength narrow-bandwidth light, compared to long-wavelength narrow-bandwidth light, administered by standard ceiling mounted LED-luminaires, affected alertness, task performance, and circadian adaptation during a simulated night shift. Similar photon density (~2.8×10^{14} photons/cm^2/s) was used for both the short-wavelength (λ_{max} = 455 nm) and the long-wavelength (λ_{max} = 625 nm) narrow-bandwidth light, with photopic illuminances of 60.8 lx and 195.9 lx, respectively. Multiple measures were used to assess subjective alertness, mood states and task performance during the simulated night shift, as well as the magnitude of the circadian phase shift following the night shift. Limited constraints and requirements were put on the participants in order to mimic naturalistic working conditions as much as possible. We employed repeated measurements to assess the alertness dynamics during the night shift. We hypothesized that high photon density short-wavelength narrow-bandwidth light, administered by standard ceiling mounted LED-luminaires, would lead to better alertness, mood and performance during the night shift, compared to a night shift with long-wavelength narrow-bandwidth light. We also hypothesized that the night shift with short-wavelength light would lead to a larger phase delay of the circadian rhythm, compared to a night shift with long-wavelength light. In addition, we investigated participants' subjective evaluation of the lighting conditions, as well as visual comfort, during the night shift.

2. Materials and Methods

2.1. Study Design

A within-subject repeated measures design was applied to investigate the effects of narrow-bandwidth light exposure (short-wavelength vs. long-wavelength) during two simulated (laboratory) night shifts (Figure 1). Participants came to the laboratory, in groups of four to eight participants, on two separate evenings to complete the night shift (23:00–06:45 h) (short-wavelength and long-wavelength light counterbalanced). The simulated night shift sessions were separated by 4 weeks. The study was conducted at a high latitude (~60° N), and during a time of year (October 2018 to March 2019) with limited daylight exposure, in order to accentuate effects of light exposure.

2.2. Participants

Thirty-four young adults participated in the study (27 females and 7 males; mean age 21.6 years, SD = 2.0 years, range 18–27 years). Six participants dropped out after the first shift, and two had their second night shift cancelled as their group (n = 2) was considered too small to carry out the night shift. Thirty-one (6 males) and 29 participants (7 males) completed the night shift in short-wavelength and long-wavelength light, respectively. Overall, 26 participants (6 males: mean age 21.6 years, SD = 1.9 years) completed both night shifts. A power analysis was conducted a priori. Expecting a medium effect size (Cohen's d = 0.5) with significance level of 0.05, power of 0.8 and correlation among repeated measures (n = 5) of 0.5 in a repeated measures within factors design (ANOVA), 21 participants were calculated to be needed [42]. The sample size complied also with the recently recommended sample size (paired t-test; n = 26) for studies investigating the alerting effects of light [43].

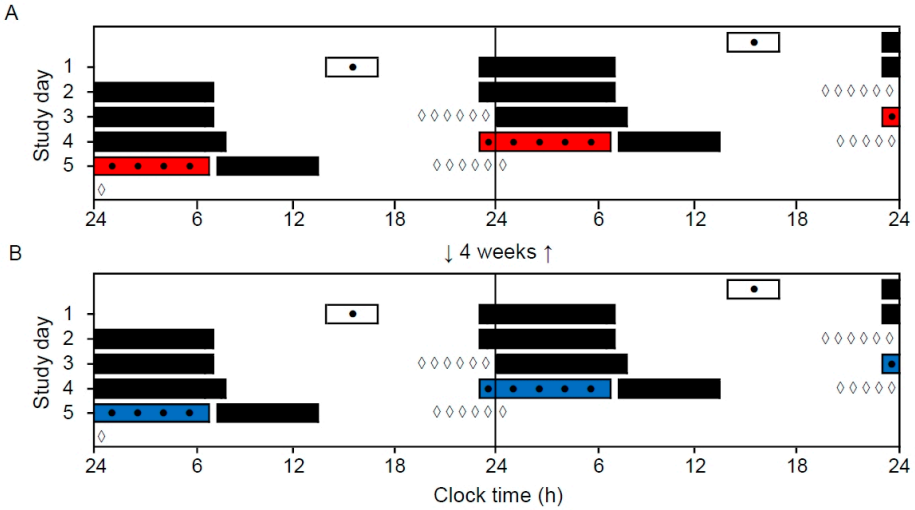

Figure 1. Double-raster plot of the simulated night shift protocol. The protocol included two simulated night shifts (from 23:00 to 06:45 h) performed in a laboratory with long-wavelength narrow-bandwidth light (**A**) and short-wavelength narrow-bandwidth light (**B**). The night shifts were separated by 4 weeks and the order of conditions was counterbalanced. White bars indicate enrollment and practice session (before the first night shift only) in the laboratory. Black bars indicate assumed sleep periods at home. Colored bars indicate night shifts in the laboratory. Black dots indicate primary test bouts including the Positive and Negative Affect Schedule (PANAS), the Karolinska Sleepiness Scale (KSS), a Psychomotor Vigilance Task (PVT), and a Digit Symbol Substitution Test (DSST). White diamonds indicate salivary dim-light melatonin sampling at home.

Participants were recruited among university students by invitation via the learning platform and/or mass e-mail. Prior to enrollment, subjects completed an online screening survey to ensure eligibility. All participants had good to excellent self-reported health and body mass index <30 kg/m^2. Participants reported no current or relevant history of psychiatric-, neurological-, cardiovascular-, lung-, sleep- and/or eye diseases/disorders, and normal color vision (also measured with the 17-plate Ishihara Test for Color Deficiency). Participants were not on medications (except some females were on oral contraceptives) and females were not pregnant or breastfeeding. None of the participants were extreme chronotypes according to the short Morningness–Eveningness Questionnaire [44], and none were engaged in night work and/or had transmeridian travel in the month prior to or during the study period. All recruited participants reported habitual sleep duration of 6–10 h per night, with habitual wake times between 06:00 and 10:00 h. These sleep criteria were set to reduce variation in participants' circadian phase, and homeostatic sleep pressure. Furthermore, the sleep criteria ensured that the participants performed the night shifts during their biological night. Adherence was confirmed by sleep diaries and wrist-actigraphy (Actiwatch 2 or Actiwatch Spectrum; Philips Respironics, The Netherlands) for three days prior to each night shift. The light sensor on the Actiwatch was also used to assess light exposure in the hours preceding the night shifts (see Table S1). Participants refrained from alcohol use three days prior to and during each night shift, caffeine use in the period from 10:00 h on the day prior to (i.e., morning coffee was allowed) and during each night shift, and tobacco/nicotine use at least 2 h prior to and during each night shift.

2.3. Procedures

Three days prior to the first night shift, eligible subjects were invited to an enrollment session. All subjects signed an informed consent form and completed a set of questionnaires and practiced the

performance tasks used in the experiment. Standard illumination (~4000 K) of approximately 200 lx at eye level (vertical plane, 120 cm height) was applied during the enrollment session. In addition, participants received the actigraph and equipment for collecting saliva samples (instructions sheet, dark sunglasses, and saliva tubes) at home. The participants slept at home with no restrictions on activities or light exposure, except during saliva sampling in the evening on the day before the night shift, and no napping was allowed on the day prior to the night shift.

The simulated night shift and light exposure (short-wavelength or long-wavelength light) started at 23:00 h and ended at 06:45 h. The first 30 min were used for adaptation and preparation, including completing questionnaires assessing visual comfort (headache and eye strain symptoms), and evaluation of the lighting conditions. At 23:30 h, the first of five main test bouts commenced, and was repeated every 90 min at 01:00, 02:30, 04:00 and 05:30 h, respectively. One test bout lasted ~20 min and included the Positive and Negative Affect Schedule (PANAS), the Karolinska Sleepiness Scale (KSS), a 10-min computerized Psychomotor Vigilance Task (PVT), and a 2-min computerized Digit Symbol Substitution Test (DSST). During testing, participants were seated at their desk space and wore noise cancelling headsets (BOSE QuietComfort 25, BOSE Corp., Framingham, MA, USA). Between the main test bouts, other tests and questionnaires were administered, such as a pegboard test, working memory, reversal learning, numerosity discrimination, and a Go/No-go test, as well as a questionnaire on evaluation of moral issues. In this paper, we report results from the main test bouts only, in addition to visual comfort and evaluation of the lighting conditions. The protocol was the same during both night shifts. Participants had several short breaks (usually 10–15 min) allowing quiet activities (e.g., reading and talking). Participants remained seated at their designated desk space for most of the time during the whole shift, except for toilet breaks, for which they had to walk through a dimly lit hallway. A researcher was present in the laboratory during the whole shift to ensure completion of tasks and adherence to the protocol. A standardized meal/snack (~200 kcal) was provided at about 02:00 and 05:00 h, and water was available ad libitum. No other foods or drinks were allowed.

Participants completing the study were compensated for their participation and inconvenience. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Norwegian Regional Committee for Medical and Health Research Ethics, health region West (No. 2016/1903). The study was preregistered, with ClinicalTrials.gov Identifier NCT03203538.

2.4. Laboratory and Light Exposure

The laboratory (30 m^2) had no windows, was air-conditioned and temperature maintained at ~22 °C. Participants were designated to one of eight similar desk spaces, separated by partition walls, with equivalent desktop computers. Computer screens were fitted with a filter foil (Metolight SFG-10; Asmetec, Kirchheimbolanden, Germany) that blocked all light wavelengths <520 nm. The room was equipped with 20 ceiling mounted LED-luminaires (Modul R 600 LED CCT/RGB MP; Glamox Luxo Lighting AB, Gothenburg, Sweden; size 60 × 60 cm), providing uniform illumination of the room. The light conditions were measured at the beginning, middle, and end of each night shift, at two desk spaces, one on each side of the room. Measurements were performed at eye level (vertical plane, 120 cm height) while seated at the desk space, using a spectroradiometer (GL Spectics 1.0 T; GL Optic, Puszczykowo, Poland). Lighting parameters (Table 1) were calculated according to the CIE S 026 Toolbox—version 1.049 [45]. The photon density was similar for the two light conditions, and both light conditions had <15 nm half-peak bandwidth (Figure 2). Note that participants' posture and gaze direction were not strictly controlled (except when engaged in the performance tasks). The light levels thus represent the approximate light exposure at eye level during most of the time in the laboratory.

Table 1. Light exposure at eye level (vertical plane) for the two light conditions.

	Short-Wavelength Narrow-Bandwidth Light	Long-Wavelength Narrow-Bandwidth Light
	Mean (SD)	**Mean (SD)**
Peak spectral irradiance (nm)	455	625
Irradiance ($\mu W/cm^2$)	125.0 (5.4)	82.6 (4.9)
Photopic illuminance (lx)	60.8 (4.0)	195.9 (10.6)
Melanopic EDI (lx)	584.5 (23.0)	4.1 (1.6)
Photon density (photons/cm^2/s)	2.9×10^{14} (1.4×10^{13})	2.6×10^{14} (1.5×10^{13})
Human photoreceptor responses (irradiance—$\mu W/cm^2$)		
S-cone-opic	97.0 (3.9)	0.2 (0.1)
M-cone-opic	23.7 (1.0)	9.5 (0.6)
L-cone-opic	14.6 (0.8)	38.3 (2.0)
Rhodopic	63.5 (2.5)	1.3 (0.2)
Melanopic	77.5 (3.1)	0.5 (0.2)

Note: Light was measured in the beginning, middle, and end of each night shift at two desk spaces. Lighting parameters computed according to the CIE S 026 Toolbox—version 1.049 [45]. EDI = equivalent daylight illuminance.

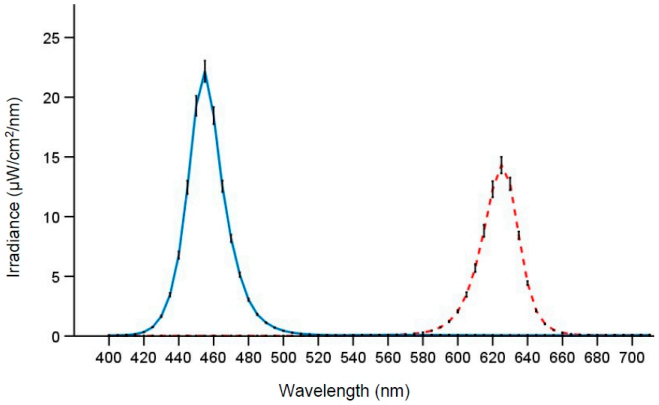

Figure 2. Spectral distribution of the short-wavelength narrow-bandwidth light (solid line) and the long-wavelength narrow-bandwidth light (dotted line). Means and SD (error bars) for measurements (vertical plane) at eye level.

The stability of the light exposure (irradiance) during the night shifts was analyzed using a linear mixed model with Group (six groups of participants) included as a random factor and Light (long-wavelength vs. short-wavelength), Time (beginning, middle or end of shift), and the interaction Light by Time entered as fixed factors. There was a significant effect of Light ($F_{1,54} = 1087.44$; $p < 0.001$) with higher irradiance of the short-wavelength light (EMM = 125; SE = 1 $\mu W/cm^2$) compared to long-wavelength light (EMM = 82; SE = 1 $\mu W/cm^2$), but there were no significant effects of Time ($F_{2,54} = 1.07$; $p = 0.351$) or the Light by Time ($F_{2,54} = 0.27$; $p = 0.765$) interaction.

2.5. Measures

2.5.1. Mood and Subjective Alertness

Positive and negative mood were measured with PANAS [46]. PANAS comprises 20 items/words describing different feelings and emotions, and participants indicated to which extent they felt a certain way at that moment on a 5-point Likert scale ranging from 1, "very slightly or not at all", to 5, "extremely". PANAS was completed at the beginning of each main test bout, and the positive

and negative affect subscales showed internal reliability of Cronbach's α = 0.92 and Cronbach's α = 0.68, respectively.

Subjective alertness/sleepiness was measured with KSS [47]. KSS comprises a 9-point Likert scale ranging from 1, "very alert", to 9, "very sleepy, fighting sleep, strenuous to keep awake". The KSS was completed at the beginning and at the end of each main test bout, and the average KSS rating for each test bout was analyzed.

2.5.2. Task Performance

Participants' vigilance and ability to sustain attention was assessed with a 10 min PVT [48,49]. The PVT is sensitive for detecting effects of sleep deprivation and shows minor aptitude and learning effects [48,49]. Participants monitored a rectangle/box on the computer screen and responded with their dominant hand by pressing the space bar when a visual stimulus (a counting timer) appeared inside the box. After each trial, a 1 s feedback on response time (RT) was provided. The interstimulus interval randomly varied from 2 to 10 s including feedback. If no response was registered after 30 s (treated as a valid trial with RT = 30,000 ms), a sound alerted the participant and a new trial began. RTs shorter than 100 ms were considered as false starts. For all PVTs performed during the night shifts (n = 300), the mean number of trials per test was 95 (SD = 6). The outcome measures reported here are the "mean 1/RT" (reciprocal RTs), "lapses" (number of RTs ≥ 500 ms) and the "mean RT500" (mean RTs with lapses excluded).

Participants also performed a 2-min DSST [50], which was administered directly following the PVT. The DSST is sensitive to changes in cognitive function, and able to detect sleep deprivation effects [50]. DSST performance improves, however, with repeated administration [50], and to minimize such learning effects the DSST was practiced once during the enrollment session, and the symbol–digit pairs were randomized across administrations. A target symbol (one of nine symbols presented in a random order) was presented at the center of the screen and had to be paired with the corresponding digit from a symbol–digit array shown at the bottom of the screen. The mouse pointer was used for selecting digits and if no response was recorded after 5 s, the next trial began. The mean number of trials per test was 76 (SD = 8), and the outcome measure derived was the "n correct" (number of correct responses).

2.5.3. Visual Comfort and Evaluation of Lighting Conditions

Visual comfort was assessed with the Headache and Eye Strain Scale (HES) [51] at the beginning (23:15 h), middle (03:15 h), and at the end (06:15 h) of each night shift. The HES questionnaire comprises 8 items/symptoms: "irritability", "headache", "eye strain", "eye discomfort", "eye fatigue", "difficulty focusing", "difficulty concentrating", and "blurred vision". Participants indicated to what extent they currently experienced the symptoms on a 4-point scale (1 = absent, 2 = slight, 3 = moderate, and 4 = severe).

Participants' subjective evaluation of the lighting conditions was assessed using a 7-point semantic differential scale questionnaire adapted from [52,53]. The questionnaire was completed at the beginning (23:15 h) and at the end (06:30 h) of each night shift. Four items comprised the subscale "pleasantness" of the lighting ("unpleasant–pleasant", "uncomfortable–comfortable", "disturbing–not disturbing" and "causing glare–not causing glare") which showed good reliability with Cronbach's α = 0.87. Four single items assessed the "clearness" ("unclear–clear"), "color" ("warm–cold"), "brightness" ("dim–bright"), and whether the lighting was "activating" ("relaxing–stimulating"). One item probed whether the light was "suitable for work" ("unsuitable for work–suitable for work"). For each of the six outcomes, the average rating for the two time points was used for analysis, as there were no differences between time of assessment.

2.5.4. Circadian Phase

Participants' circadian phase was assessed before and after each night shift by measuring salivary dim light melatonin onset (DLMO). Baseline DLMO was sampled in the evening on the day before each night shift, while the final DLMO was sampled in the evening on the day after each night shift. Participants provided hourly saliva samples at home (six samples each evening), using Salivette tubes (Sarstedt AG & CO, Nümbrecht, Germany). Sampling of baseline DLMO started 4 h before and lasted until 1 h after the participants' usual bedtime. Relative to baseline DLMO sampling, the time of final DLMO sampling was delayed by 1 h (hence the last sampling was 2 h after usual bedtime). A similar protocol as described in a previous study was applied [54]. To ensure dim light during sampling, participants wore dark sunglasses (Uvex Athletic ISO 9001, Uvex Winter Holding GmbH & Co., Fürth, Germany; and/or Uvex Genesis S3208 Infra-dura 5.0, Honeywell, Charlotte, NC, USA) from 1 h before and during the whole sampling period. These glasses' lenses reduce light intensity to <1% [54]. Before delivery to the laboratory for storage at −70 °C, participants were instructed to label the samples with clock time and store them in their domestic refrigerator (4 °C).

The saliva samples were assayed with an enzyme-linked immunosorbent assay kit (EK-DSM, Bühlman Laboratories, Schönenbuch, Switzerland) with a detection limit of 0.5 pg/mL and a functional sensitivity of 1.6–20.5 pg/mL. A Wallac 1420 Multilabel counter (Perkin Elmer Inc., Waltham, MA, USA) was used to analyze the samples. The inter-assay variation was 18.4% and 14.8% for the low and high quality control, respectively. The mean (SD) melatonin value was 4.4 (0.8) and 13.7 (2.0) pg/mL for the low and high quality control, respectively. The DLMO was set as the clock time when salivary melatonin concentration reached 4 pg/mL, using linear interpolation between adjacent samples [55]. If melatonin concentration during sampling reached 3 pg/mL, but not 4 pg/mL, linear extrapolation was used. The magnitude of the phase shift was calculated as the difference between baseline DLMO and final DLMO for each individual. As an estimate of the temperature minimum (Tmin), 7 h was added to the baseline and final DLMO [27].

Due to missing DLMO data, the circadian phase shift could not be calculated for all participants. After the night shift in long-wavelength light, phase shifts were estimated for 22 (76%) of 29 participants, while after the night shift in short-wavelength light, phase shifts were estimated for 19 (61%) of 31 participants. For the long-wavelength light condition, one participant did not reach 3 pg/mL during final sampling, four had melatonin levels exceeding 4 pg/mL for all samples at baseline and/or final DLMO sampling, and two participants did not provide saliva samples. For the short-wavelength light condition, three participants did not reach 3 pg/mL during final sampling, eight had melatonin levels exceeding 4 pg/mL for all samples at baseline and/or final DLMO sampling, and one did not perform the final sampling.

2.6. Statistical Analysis

Participant characteristics were described by means and standard deviations (SD). To assess the effects of light exposure, Linear Mixed Model (LMM) analyses and Generalized Linear Mixed Model (GLMM) analyses were performed. For positive mood, negative mood, KSS, PVT mean 1/RT and mean RT500, and the DSST *n* correct (separate analyses per variable), three LMM models, using maximum likelihood estimation, were performed for each of the variables: (1) A random effect model with Participant included as a random effect, (2) a main effects model with Light (short-wavelength vs. long-wavelength) and Time (23:30 vs. 01:00, 02:30, 04:00 and 05:30 h) entered in the model as fixed factors, and (3) an interaction effect model with the Light by Time interaction also included as a fixed factor. For all variables, the main effects model had a better model fit, as assessed with a Likelihood Ratio Test (LRT), than the random effect model. For variables with a significant Light by Time interaction, the LRT indicated that the interaction effect model had the best model fit. The LRT was performed by comparing the difference in −2 times the log of the likelihood between successive models following a chi-square distribution, using degrees of freedom equal to the difference in the number of parameters between the compared models. The normality of the residuals from the interaction effect

models were assessed with Shapiro–Wilk tests and normality plots to confirm that assumptions were met. Post-hoc comparisons were conducted using Bonferroni corrections, and the estimated marginal means (EMM) and standard errors (SE) are reported. R-squared (R^2) was calculated representing the proportion of reduction in variance of the residuals (this measure can also have negative values), and R^2 for the interaction effect models are reported.

PVT lapses were analyzed using GLMM models, with a negative binominal distribution, as this is a count variable showing overdispersion. A similar procedure as described above (random-, main- and interaction effect models) was applied. The LRT approach for assessing model fit is not appropriate for the GLMM analyses, as restricted maximum likelihood estimation is used. Instead, the Akaike's information criterion (AIC) and the Schwarz's Bayesian criterion (BIC) were used for comparison of model fit (smallest values were preferred), and accordingly, the interaction effects model had the best fit.

The HES symptoms, and the items probing evaluation of the lighting conditions, were analyzed using LMMs as described above. However, there were only three time points (23:15, 03:15 and 06:15 h) for the HES' Time factor, and for evaluation of lighting conditions there was no time factor (nor interaction) entered into the LMM models.

The magnitude of the phase shift was analyzed using LMMs with Participant as a random effect, and Light (short-wavelength vs. long-wavelength) included as a fixed factor, employing similar settings and procedures as described above. To investigate whether there were differences in baseline DLMO between the conditions, paired samples *t*-tests were used. Pearson's product–moment correlation coefficients were calculated to assess whether baseline DLMO was related to the phase shift magnitude.

Statistical analyses were performed using IBM SPSS Statistics, version 25 (IBM Corp., Endicott, NY, USA).

3. Results

3.1. Mood and Subjective Alertness

3.1.1. PANAS: Effects on Mood

Analyses of positive mood and negative mood indicated no significant main effects of Light, but there was a significant main effect of Time for both measures (Table 2). Positive mood was reduced at 01:00, 02:30, 04:00 and 05:30 h ($p < 0.001$, all) compared to 23:30 h. Negative mood was reduced at 02:30 h ($p = 0.002$) compared to 23:30 h. For positive mood, there was no significant Light by Time interaction effect (Figure 3A). For negative mood, there was a significant Light by Time interaction effect, and post-hoc comparisons revealed increased negative mood in short-wavelength light at 23:30 h (Figure 3B).

3.1.2. KSS: Effects on Subjective Sleepiness

For KSS, there were significant main effects of Light with reduced sleepiness in short-wavelength light, and Time with increased sleepiness at 01:00, 02:30, 04:00 and 05:30 h ($p < 0.001$, all) compared to 23:30 h (Table 2). There was also a significant Light by Time interaction effect, with post-hoc comparisons showing reduced sleepiness in short-wavelength light in the middle and later parts of the night shift (Figure 3C).

Table 2. Effects of light condition and time on mood, subjective sleepiness, task performance and visual comfort.

	Long-Wavelength Light	Short-Wavelength Light	Light		Time		Light by Time		
	EMM (SE)	EMM (SE)	*F* (*df*)	*p*	*F* (*df*)	*p*	*F* (*df*)	*p*	R^2
PANAS (10–50 (extremely))									
Positive mood	19.63 (0.87)	20.22 (0.86)	1.13 (1, 278)	0.289	56.81 (4, 267)	<0.001	1.57 (4, 267)	0.182	0.28
Negative mood	11.55 (0.31)	11.74 (0.31)	0.99 (1, 278)	0.320	3.93 (4, 267)	0.004	3.24 (4, 267)	0.013	0.05
Sleepiness (KSS, 1–9 (sleepy))	6.97 (0.21)	6.28 (0.21)	25.32 (1, 278)	<0.001	59.23 (4, 266)	<0.001	3.61 (4, 266)	0.007	0.30
Psychomotor vigilance task									
Mean 1/RT	2.82 (0.08)	2.97 (0.08)	18.36 (1, 272)	<0.001	32.21 (4, 266)	<0.001	3.29 (4, 266)	0.012	0.14
Mean RT500	342.79 (5.46)	332.40 (5.44)	25.24 (1, 270)	<0.001	40.97 (4, 266)	<0.001	4.04 (4, 266)	0.003	0.14
Number of lapses (RTs ≥ 500 ms) [a]	6.95 (1.49)	4.82 (1.09)	6.60 (1, 290)	0.011	37.41 (4, 290)	<0.001	2.68 (4, 290)	0.032	-
Digit symbol substitution test (*n* correct)	73.50 (1.32)	76.35 (1.31)	18.17 (1, 273)	<0.001	8.48 (4, 265)	<0.001	1.58 (4, 265)	0.180	0.08
Headache and eye strain scale (1–4 (severe))									
Irritability	1.71 (0.12)	1.70 (0.12)	0.01 (1, 155)	0.928	7.41 (2, 147)	0.001	2.78 (2, 147)	0.065	0.05
Headache	1.80 (0.11)	1.58 (0.11)	7.14 (1, 156)	0.008	18.45 (2, 147)	<0.001	0.57 (2, 147)	0.568	0.11
Eye strain	2.73 (0.12)	2.44 (0.12)	8.33 (1, 157)	0.004	39.45 (2, 146)	<0.001	2.08 (2, 146)	0.129	0.22
Eye discomfort	2.50 (0.14)	2.22 (0.14)	7.18 (1, 154)	0.008	29.75 (2, 146)	<0.001	3.82 (2, 146)	0.024	0.15
Eye fatigue	2.86 (0.11)	2.49 (0.11)	14.18 (1, 158)	<0.001	86.07 (2, 145)	<0.001	3.97 (2, 145)	0.021	0.39
Difficulty focusing	2.72 (0.13)	2.45 (0.13)	7.72 (1, 154)	0.006	56.07 (2, 145)	<0.001	2.05 (2, 145)	0.132	0.25
Difficulty concentrating	2.74 (0.11)	2.39 (0.11)	11.27 (1, 160)	0.001	74.03 (2, 147)	<0.001	1.45 (2, 147)	0.238	0.38
Blurred vision	2.06 (0.14)	1.82 (0.13)	6.43 (1, 154)	0.012	13.83 (2, 146)	<0.001	1.54 (2, 146)	0.219	0.07

Note: Variables analyzed using linear mixed model analyses. [a] Analyzed using generalized linear mixed models. R^2 is the proportion of reduction in variance of the residuals between a random effects model and the interaction effects model. EMM = estimated marginal mean; SE = standard error; *df* = degrees of freedom; PANAS = Positive and Negative Affect Schedule; KSS = Karolinska Sleepiness Scale; RT = response time.

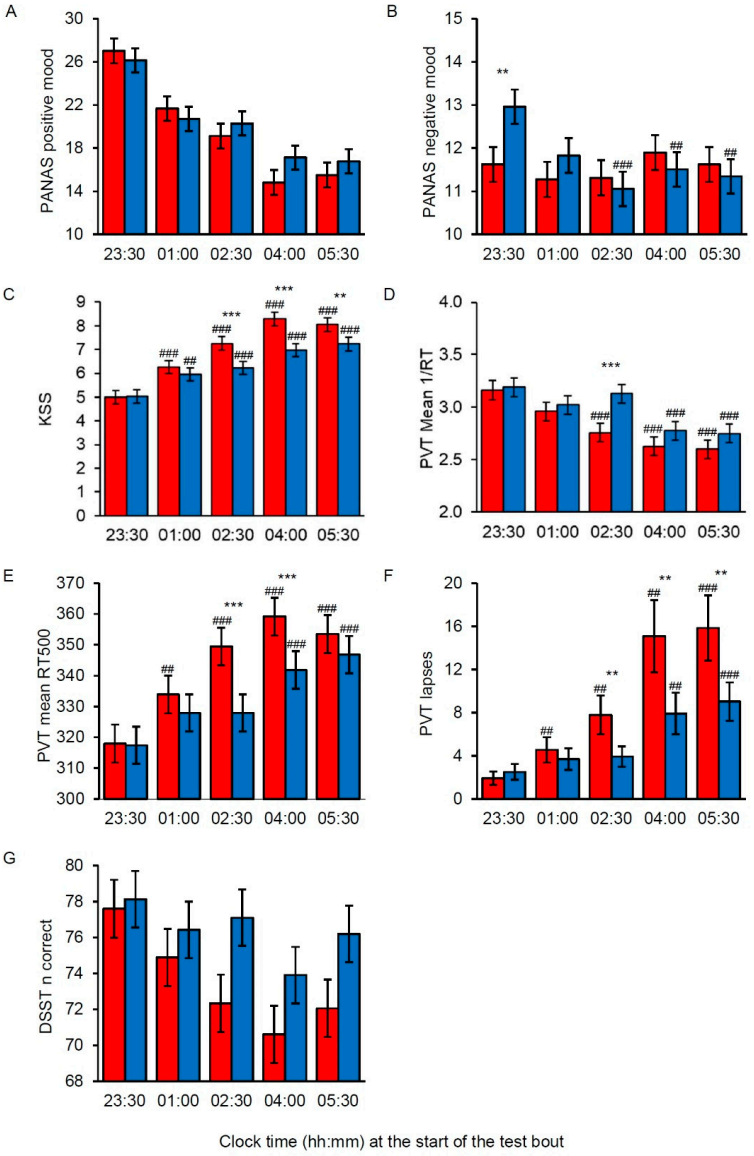

Figure 3. Mood, sleepiness and performance during a simulated night shift in long-wavelength narrow-bandwidth light (red bars) and short-wavelength narrow-bandwidth light (blue bars). The bars represent estimated marginal means with error bars indicating standard error. (**A**) Positive mood assessed with the Positive and Negative Affect Schedule (PANAS). (**B**) Negative mood assessed with PANAS. (**C**) Subjective sleepiness assessed with the Karolinska Sleepiness Scale (KSS). (**D**) Reciprocal response times (mean 1/RT) on the Psychomotor Vigilance Task (PVT). (**E**) RTs excluding lapses (mean RT500) on the PVT. (**F**) Number of lapses (RTs ≥ 500 ms) on the PVT. (**G**) Number of correct responses on the Digit Symbol Substitution Test (DSST). Significant differences indicated for variables with a significant Light by Time interaction only. Number symbols (#) indicate significant difference compared to the first test bout (23:30 h), and asterix symbols (*) indicate significant difference between light conditions. ##; ** = $p < 0.01$, ###; *** = $p < 0.001$.

3.2. Task Performance

3.2.1. PVT: Effects on Sustained Attention

Analysis of both mean 1/RT and mean RT500 revealed significant main effects of Light with faster RTs in short-wavelength light, and Time with slower RTs at 01:00 (mean 1/RT: $p < 0.001$; mean RT500: $p = 0.005$), 02:30, 04:00 and 05:30 h ($p < 0.001$, all) compared to 23:30 h (Table 2). There were also significant Light by Time interaction effects, and post-hoc comparisons revealed faster RTs in short-wavelength light in the middle and later parts of the night shift (Figure 3D,E). Results were similar for the number of lapses, with significant main effects of Light with fewer lapses in short-wavelength light, and Time with more lapses at 01:00 ($p = 0.002$), 02:30 ($p = 0.001$), 04:00 and 05:30 h ($p < 0.001$, both) compared to 23:30 h (Table 2). There was also a significant Light by Time interaction effect, with post-hoc comparisons showing fewer lapses in short-wavelength light in the middle and later parts of the night shift (Figure 3F).

3.2.2. DSST: Effects on Number of Correct Responses

For the DSST n correct, there were main effects of Light with more correct responses in short-wavelength light, and Time with fewer correct responses at 02:30 ($p = 0.018$), 04:00 ($p < 0.001$) and 05:30 h ($p = 0.002$) compared to 23:30 h (Table 2). There was no significant Light by Time interaction effect for the DSST (Figure 3G).

3.3. Visual Comfort and Evaluation of Lighting Conditions

3.3.1. Visual Comfort: Effects on Headache and Eye Strain Symptoms

There were significant main effects of Light for all symptom categories, except irritability, with reduced symptoms in short-wavelength light (Table 2). For all categories there were significant main effects of Time with increased symptoms at 03:15 h (irritability: $p = 0.032$; blurred vision: $p = 0.263$; all other $p < 0.001$) and at 06:15 ($p \leq 0.001$, all) compared to 23:15 h. For eye discomfort and eye fatigue, there were significant Light by Time interaction effects, and post-hoc comparisons showed reduced symptoms in short-wavelength light in the middle and late parts of the night shift (Figure 4). There were no significant Light by Time interaction effects for irritability, headache, eye strain, difficulty focusing, difficulty concentrating or blurred vision (Figure 4).

3.3.2. Subjective Evaluation of the Lighting Conditions

Evaluation of the lighting conditions revealed a significant main effect of Light for color ($F_{1,60} = 124.89$; $p < 0.001$; $R^2 = 0.68$), with short-wavelength light (EMM = 5.58, SE = 0.20) evaluated as colder than long-wavelength light (EMM = 2.43, SE = 0.20), brightness ($F_{1,60} = 8.78$; $p = 0.004$; $R^2 = 0.13$), with short-wavelength light (EMM = 4.60, SE = 0.23) evaluated as brighter than long-wavelength light (EMM = 3.64, SE = 0.23), and whether the light was activating ($F_{1,60} = 13.56$; $p < 0.001$; $R^2 = 0.18$), with short-wavelength light (EMM = 4.55, SE = 0.17) evaluated as more activating than long-wavelength light (EMM = 3.64, SE = 0.18). Note that for these variables, models were run without the random intercept as an error showed that the Hessian matrix was not positive definite, suggesting redundant covariance parameters. There was no significant main effect of Light for pleasantness ($F_{1,30} = 1.31$; $p = 0.262$; $R^2 = 0.01$), with similar estimates for short-wavelength light (EMM = 4.09, SE = 0.22) and long-wavelength light (EMM = 3.81, SE = 0.21), clearness ($F_{1,31} = 0.00$; $p = 0.953$; $R^2 < 0.01$), with similar estimates for short-wavelength light (EMM = 4.15, SE = 0.20) and long-wavelength light (EMM = 4.14, SE = 0.20), and whether the lighting was considered suitable for work ($F_{1,29} = 2.50$; $p = 0.125$; $R^2 = -0.26$), with similar estimates for short-wavelength light (EMM = 3.75, SE = 0.26) and long-wavelength light (EMM = 3.38, SE = 0.26).

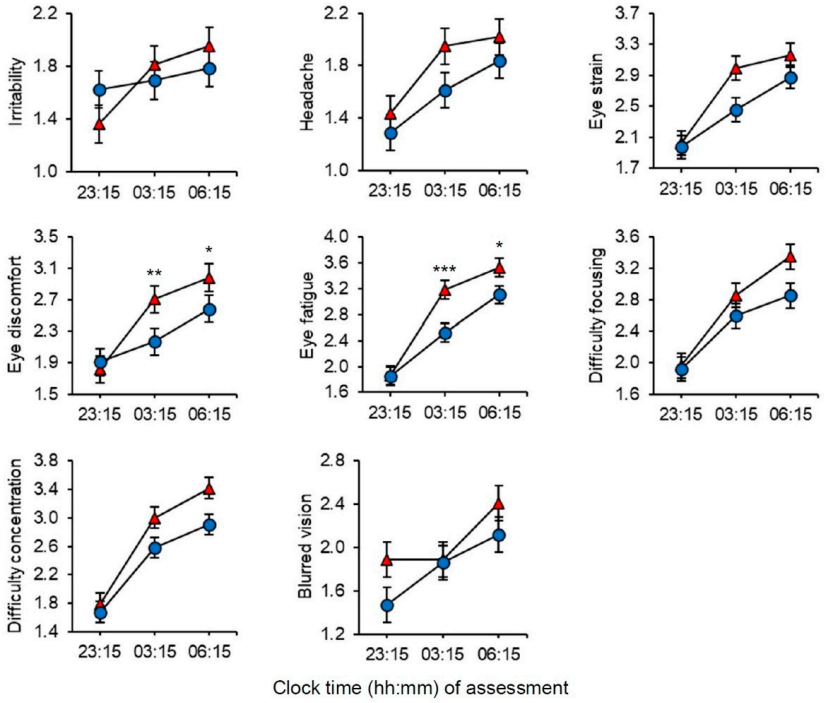

Figure 4. Visual comfort assessed with the headache and eye strain scale (1–4 (severe)) during a simulated night shift in long-wavelength narrow-bandwidth light (triangles) and short-wavelength narrow-bandwidth light (circles). Data points are the estimated marginal means with error bars indicating standard error. Significant differences between light conditions indicated for variables with a significant Light by Time interaction only. * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$.

3.4. Circadian Phase

For long-wavelength light, baseline DLMO (n = 26; mean = 21:42 h, SD = 1:09 h) ranged from 19:05 to 00:01 h, and final DLMO (n = 22; mean = 22:25 h, SD = 1:15 h) ranged from 20:35 to 01:00 h (Figure 5A). For short-wavelength light, baseline DLMO (n = 27; mean = 21:23 h, SD = 1:13 h) ranged from 19:08 to 00:08 h, and final DLMO (n = 20; mean = 22:46 h, SD = 1:49 h) ranged from 19:34 to 03:02 h (Figure 5B). There was no significant difference in baseline DLMO for the 22 participants with complete baseline DLMO estimates (short-wavelength light: mean = 21:36 h, SD = 1:09 h, long-wavelength light: mean = 21:46 h, SD = 1:14 h; $t_{21} = 0.91$; $p = 0.375$). A similar result was found when analyzing baseline DLMO for the 12 participants with complete baseline and final DLMO estimates in both light conditions (short-wavelength light: mean = 21:26 h, SD = 0:59 h; long-wavelength light: mean = 21:41 h, SD = 1:11 h, $t_{11} = 1.03$; $p = 0.324$).

For circadian phase shift, there was a significant main effect of Light ($F_{1,24} = 5.33$; $p = 0.030$; $R^2 = 0.11$) indicating larger phase shift (delay) after a night shift in short-wavelength light (EMM = 1:26 h, SE = 0:16 h) compared to long-wavelength light (EMM = 0:36 h, SE = 0:15 h). There was no significant correlation between the magnitude of the phase shift and baseline DLMO for either short-wavelength ($r = 0.33$; $p = 0.167$) or long-wavelength ($r = -0.33$; $p = 0.131$) light.

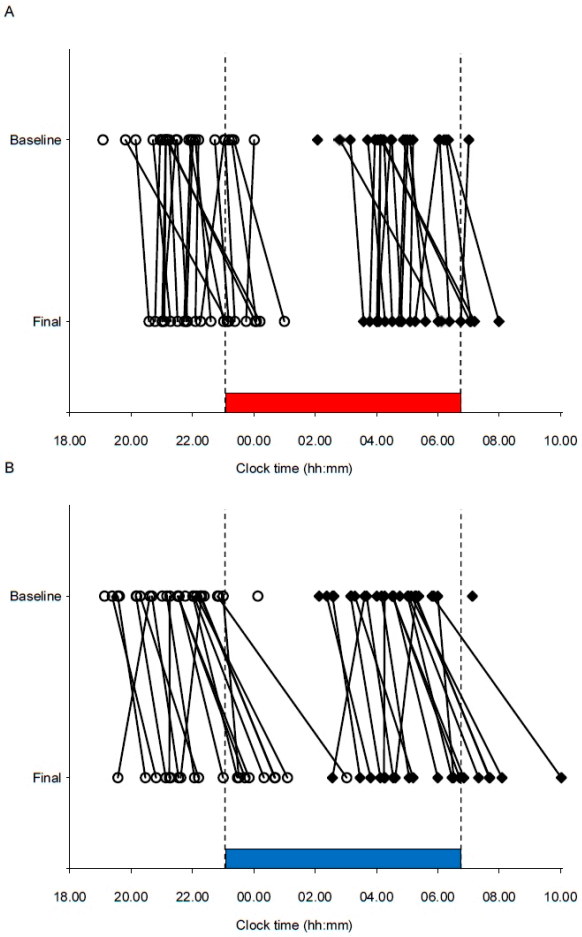

Figure 5. Phase markers for individual participants before (Baseline) and after (Final) a simulated night shift in (**A**) long-wavelength narrow-bandwidth light and (**B**) short-wavelength narrow-bandwidth light. Open circles indicate salivary dim light melatonin onset (DLMO) for each participant. Filled diamond squares indicate estimated temperature minimum (DLMO + 7 h) for each participant. Lines are drawn between the baseline and final markers for each participant. The vertical dotted lines and colored bars indicate the start and end times of the night shift and light exposure (23:00–06:45 h).

4. Discussion

In this study, we investigated the effects of nocturnal short-wavelength narrow-bandwidth light (λ_{max} = 455 nm) compared to long-wavelength narrow-bandwidth light (λ_{max} = 625 nm) with similar photon density (~2.8×10^{14} photons/cm^2/s), administered by standard ceiling mounted LED-luminaires, during a simulated night shift. To our knowledge, this study is the first to employ such LED-based light conditions during night work. As expected, subjective sleepiness increased, positive mood was reduced and task performance deteriorated during the night shift in both light conditions. However, with short-wavelength light the increase in sleepiness and the deterioration of task performance across the night shift was less severe than with long-wavelength light. Overall, our hypothesis of better alertness and performance during a night shift with short-wavelength narrow-bandwidth light, compared to long-wavelength narrow-bandwidth light, was supported. We did, however, not find

beneficial effects of short-wavelength light on participants' mood states. Participants' melatonin onset was mainly phase delayed after the night shifts, and there was a significantly larger phase delay after the night shift with short-wavelength light compared to long-wavelength light. Hence, our hypothesis of a greater phase delay with short-wavelength narrow-bandwidth light was supported. There were no statistically significant differences between the light conditions in terms of participants' evaluation of its pleasantness and suitability for work. However, we found evidence of improved visual comfort with short-wavelength light compared to long-wavelength light.

The results on subjective sleepiness and task performance showed very similar patterns, with beneficial effects of short-wavelength light emerging from 02:30 h onwards. PVT performance was better in short-wavelength light, both in terms of generally faster RTs (mean 1/RT), faster RTs in the optimal domain (RT500), and fewer attentional lapses (i.e., slow RTs) than in long-wavelength light. A similar pattern was observed for DSST performance, albeit no statistically significant interaction effect was found. Previous studies have reported beneficial effects of late evening and nocturnal exposure to short-wavelength light on alertness level and/or task performance [14,15,18]. However, as discussed in the introduction, those studies employed substantially lower photon densities than the current study. As noted, the previous studies were highly controlled laboratory trials using special lighting set-ups. The current results thus add to previous findings showing that short-wavelength narrow-bandwidth light, administered by standard ceiling mounted LED-luminaires in a naturalistic setting, also elicits alerting and performance enhancing responses, compared to long-wavelength narrow-bandwidth light. In addition, the results indicate that these effects can be achieved using higher photon densities than previously reported. As noted in the introduction, long-wavelength light may also elicit alerting responses compared with dark conditions. In the afternoon, long-wavelength narrow-bandwidth light (λ_{max} = 630 nm) improved alertness, while short-wavelength narrow-bandwidth light (λ_{max} = 470 nm) did not improve alertness, compared to darkness [23]. These findings do not match the alerting effect of nocturnal short-wavelength light, compared to long-wavelength light, in the present study, likely due to the role of melatonin suppression during nighttime. We did not have an additional night shift in dim light or in standard light conditions, hence the alerting effects of our light conditions cannot be compared to dim light or standard light conditions.

Regarding mood states, the positive mood indicator showed no statistically significant difference between the light conditions. For negative mood, there was a significantly higher score in short-wavelength light compared to long-wavelength light on the first assessment at 23:30 h, a difference that vanished in the subsequent sessions. It is not clear why this difference occurred, but it is possible that exposure to short-wavelength light initially had a negative impact on mood, and that longer than 30 min adaptation to the light is needed to reduce this effect. We did not assess mood prior to the light exposure. Hence, it is possible, yet unlikely, that there was a difference in negative mood prior to the night shift between the two light conditions. Thus, we cannot rule out that the short-wavelength light actually reduced the negative mood score compared to the long-wavelength light.

In terms of circadian phase, the significantly larger phase delay observed with short-wavelength light shows that overall, the participants' circadian rhythm became more strongly entrained to night work after a night shift in short-wavelength light compared to long-wavelength light. However, the individual differences in circadian responses indicate that factors other than the light are also at play, such as differences in sensitivity to light [56]. Notably, following the night shift, the melatonin rhythm of a few participants showed the opposite phase shifting response (i.e., phase advance), although they had a similar initial melatonin onset time. Since the light exposure in the current study was kept constant during the whole shift, most participants were also exposed to light after their estimated Tmin, in the phase advance part of the participants' phase response curves (PRC) to light [57,58]. As circadian responses are sensitive to short-wavelength light, short-wavelength light exposure after Tmin may have attenuated the phase delay to a larger degree than long-wavelength light, and/or caused a phase advance of the melatonin rhythm. Nevertheless, the current findings are in line with previously reported data showing a greater phase delay with short-wavelength narrow-bandwidth

light administered before Tmin [11]. Individual differences in phase shifting responses to light have also been noted previously [11], and a recent study found that variations in the distribution of daily light exposure relative to the PRC accounted for a large portion of the variable rates of circadian adaptation among real night workers [59].

Participants evaluated the short-wavelength light condition as colder, brighter, and more activating than the long-wavelength light. The opinion of the short-wavelength light being brighter seems somewhat remarkable, as the photopic illuminance of the long-wavelength light (195.9 lx) was substantially higher than the short-wavelength light (60.8 lx). Nevertheless, similar findings were reported in a study comparing brightness experiences of light with high and low correlated color temperature [53]. This phenomenon probably reflects difficulties in subjectively comparing the brightness of light stimuli of different colors [60]. In addition, it has been shown that brightness perception has a short-wavelength spectral sensitivity that increases with increasing light levels [61], which could explain the greater brightness perception of the short wavelength light in our study. The evaluation of short-wavelength light as more activating corroborates the alerting and performance enhancing effects of short-wavelength light.

In terms of visual comfort, the increase in HES symptoms during the shift suggests that neither the short-wavelength nor the long-wavelength light was ideal, although there was improved visual comfort with short-wavelength light. However, we cannot discern between these effects being related to the light conditions alone or the night work itself. Still, the evidently reduced symptoms with short-wavelength light compared to long-wavelength light, and the relatively large amount of explained variance for some of the symptoms (e.g., eye fatigue), suggests that the light conditions are of importance. Note that compared to HES symptoms reported during daytime office hours [51], the severity for most symptoms in the current study was considerably larger in both light conditions in the middle and later parts of the night shift. The previous study of office workers did not investigate narrow-bandwidth light but compared strongly blue-enriched light (17,000 K) with standard white light (4000 K) [51]. Improved visual comfort with blue-enriched light was found among the office workers [51] and this was suggested to be related to pupil responses driven by melanopsin and the ipRGCs [13], and it was further suggested that greater pupil constriction may have contributed to the improved visual comfort. Similar effects may explain the findings in the current study as the short-wavelength light triggered a far higher melanopsin stimulation than the long-wavelength light. Recently, it was suggested that the mechanisms for light exacerbating migraine headaches can be explained by responses of cone driven retinal pathways [62]. In the current study, both the short-wavelength and long-wavelength light stimulated the cones, but the long-wavelength light had more than twice the L-cone-opic (i.e., long wavelength cone) irradiance than the short-wavelength light, with 38.3 and 14.6 $\mu W/cm^2$, respectively. Hence, this difference may also contribute to the increased HES symptoms experienced with the long-wavelength light.

In the present study, subjective measures and task performance assessments were repeated throughout the night shift in order to investigate the effects of short-wavelength and long-wavelength narrow-bandwidth light on participants' functioning. A crossover design was used to control for interindividual differences in the dependent variables and interindividual variability in responses to light [56]. To ensure no crossover effects, counterbalancing and a four-week washout period between night shifts were applied. Unfortunately, some participants did not complete both night shifts (i.e., both light conditions). However, despite missing data, compared to many previous trials, the current study included a relatively large sample size in concordance with recent recommendations [43]. In addition, the statistical analysis strategy (using LMM and GLMM analyses) allowed for missing values in the dataset without excluding cases completely. Nevertheless, caution should be taken, particularly when interpreting the circadian phase shift data, as there was a relatively large amount of missing DLMO estimates. Participants were not extreme chronotypes, not allowed to nap, and were selected based on sleep timing and duration criteria. Bearing in mind the use of a crossover design, differences in homeostatic sleep pressure likely did not have significant impact on the results. It should be noted that

the current sample consisted of relatively young adults. Thus, it is not clear whether the current results can be generalized to other populations and age groups. It is known that with older age there are retinal changes, i.e., yellowing of the lens, and light exposure can differentially impact nonvisual responses during extended wakefulness in young and older individuals [63]. In addition, since males have shown greater nonvisual responses to light and differ in their opinion of lighting compared to females [64], a sample with a more even sex distribution could have given rise to somewhat different results.

The present study demonstrates a novel use of ceiling mounted LED-luminaires for administering narrow-bandwidth light conditions during simulated night work. Furthermore, we employed relatively high photon densities of light, which may be realistic for real-life work situations. However, the practical relevance for night workers remains debatable. Ambient narrow-bandwidth lighting alters visibility and color rendering (i.e., color appearance of the surroundings), hence for many workplaces the narrow-bandwidth lighting employed in the present study may not be feasible. The novel way of administering the narrow-bandwidth light conditions in the current study, however, offers new opportunities for illumination that need further investigation in terms of feasibility for specific workplaces and settings. A concern with short-wavelength light, in particular, relates to the potential negative impact of light at night [34,35], e.g., melatonin suppression and circadian disturbance. The present results indicate strong phase shifting effects of the short-wavelength light. While such effects may be practical for permanent night workers, they may at the same time be regarded as unwanted effects for rotating night workers. Another consideration, not assessed in the present paper, is the impact of light interventions on sleep and recovery after night work, as sleep disturbances are one of the main issues with night work [24,25]. Thus, there is a need to consider which effects of light are most desired in specific work situations and settings, particularly for night workers.

We did not thoroughly control participants' light exposure prior to the night shifts, as has been done in previous laboratory studies. Light exposure in the hours (18:00–22:45) preceding the night shifts was monitored by the light sensor on the actigraph device, indicating no significant difference between conditions. Prior light history is known to affect nonvisual light responses, including the alerting response [65]; hence, this may have also had an impact in the current study. However, the relatively high latitude and time of year ensured limited daylight exposure in the hours preceding the night shifts. Furthermore, we did not employ individually tailored light exposure, as suggested by a recent study [30]. Due to the inter-individual differences in circadian phase timing, the fixed work schedule, and uniformly lit work environment, the light exposure occurred at different circadian times for different participants. Hence, individually tailored light exposure would likely lead to even larger phase shifting effects than observed. We aimed to keep the study similar to a real-life night work setting and put limited restraints on the participants during their spare time. It can thus be viewed as a strength that our findings were in agreement with the previous highly controlled laboratory studies showing alerting and phase shifting effects of duly timed short-wavelength narrow-bandwidth light. A limitation with the present study was that the participants did not complete a baseline test bout just prior to the light exposure. Thus, we cannot exclude that variation in the assessed parameters (PANAS, KSS, PVT, and DSST) may have existed prior to light exposure, and that the first 30 min of light exposure affected the parameters. However, considering the repeated measures design and counterbalancing, it is unlikely that this greatly distorted the results.

Future studies should investigate the possibility of providing individually tailored light exposure, using standard ceiling mounted LED-luminaires, e.g., by programming luminaires to provide favorable light exposure at individual workplaces. Furthermore, there is a need for more studies to assess the amount of melatonin suppression throughout the night shift under different light conditions.

5. Conclusions

The current study revealed beneficial effects of exposure to short-wavelength narrow-bandwidth light (λ_{max} = 455 nm), compared to photon matched (~2.8×10^{14} photons/cm^2/s) long-wavelength narrow-bandwidth light (λ_{max} = 625 nm), on subjective alertness and task performance during a

simulated night shift. Moreover, the participants' melatonin onset was more phase delayed in short-wavelength light compared to long-wavelength light. It was demonstrated that short-wavelength narrow-bandwidth light can improve alertness and performance, as well as strengthen circadian phase shifting, during simulated night work using standard ceiling mounted LED-luminaires and relatively high light levels. Participants evaluated both light conditions as moderately pleasant and moderately suitable for work, albeit visual comfort was higher in short-wavelength light compared to long-wavelength light. These results show that standard LED-luminaires can be used to administer short-wavelength narrow-bandwidth light with the potential to improve alertness and performance among night workers. However, more studies are needed to validate these findings, e.g., in different populations, and to investigate the applicability of such light conditions in real-life workplaces. There is a need to further study LED-based lighting in order to develop lighting recommendations for night workers.

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III

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Blue-Enriched White Light Improves Performance but Not Subjective Alertness and Circadian Adaptation During Three Consecutive Simulated Night Shifts

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Use of blue-enriched light has received increasing interest regarding its activating and performance sustaining effects. However, studies assessing effects of such light during night work are few, and novel strategies for lighting using light emitting diode (LED) technology need to be researched. In a counterbalanced crossover design, we investigated the effects of a standard polychromatic blue-enriched white light (7000 K; ∼200 lx) compared to a warm white light (2500 K), of similar photon density (∼1.6 × 10^{14} photons/cm^2/s), during three consecutive simulated night shifts. A total of 30 healthy participants [10 males, mean age 23.3 (*SD* = 2.9) years] were included in the study. Dependent variables comprised subjective alertness using the Karolinska Sleepiness Scale, a psychomotor vigilance task (PVT) and a digit symbol substitution test (DSST), all administered at five time points throughout each night shift. We also assessed dim-light melatonin onset (DLMO) before and after the night shifts, as well as participants' opinion of the light conditions. Subjective alertness and performance on the PVT and DSST deteriorated during the night shifts, but 7000 K light was more beneficial for performance, mainly in terms of fewer errors on the PVT, at the end of the first- and second- night shift, compared to 2500 K light. Blue-enriched light only had a minor impact on PVT response times (RTs), as only the fastest 10% of the RTs were significantly improved in 7000 K compared to 2500 K light. In both 7000 and 2500 K light, the DLMO was delayed in those participants with valid assessment of this parameter [*n* = 20 (69.0%) in 7000 K light, *n* = 22 (78.6%) in 2500 K light], with a mean of 2:34 (*SE* = 0:14) and 2:12 (*SE* = 0:14) hours, respectively, which was not significantly different between the light conditions. Both light conditions were positively rated, although participants found 7000 K to be more suitable for work yet evaluated 2500 K light as more pleasant. The data indicate minor, but beneficial, effects of 7000 K

light compared to 2500 K light on performance during night work. Circadian adaptation did not differ significantly between light conditions, though caution should be taken when interpreting these findings due to missing data. Field studies are needed to investigate similar light interventions in real-life settings, to develop recommendations regarding illumination for night workers.

Clinical Trial Registration: www.ClinicalTrials.gov, identifier NCT03203538.

Keywords: night work, alertness, performance, Fatigue, countermeasures, light, light emitting diode

INTRODUCTION

Night work is a common type of shift work (Eurofound, 2017), associated with a range of adverse health effects (Kecklund and Axelsson, 2016), as well as increased risk of occupational injury (Fischer et al., 2017). A major challenge with night work concerns increased sleepiness and deterioration of performance, especially vigilant attention, during the shifts (Lim and Dinges, 2008; Åkerstedt and Wright, 2009; Ganesan et al., 2019; Mulhall et al., 2019). The alertness and performance decrements reflect misalignment of the circadian timing system, as well as homeostatic build-up of sleep need due to extended time in wakefulness (Santhi et al., 2007; Borbely et al., 2016; Mulhall et al., 2019).

Circadian rhythms reflect processes displaying endogenous oscillations around 24 h. They play a key role in when we sleep and when we are awake, as well as in body temperature levels, secretion of several hormones (e.g., melatonin, cortisol) and in our cognitive performance throughout the day (Rajaratnam and Arendt, 2001). Circadian rhythms are controlled and coordinated by the pacemaker located in the suprachiasmatic nuclei (SCN), and the light-dark cycle provides the strongest cue for entraining the SCN to the external day and night (Roenneberg and Foster, 1997). Artificial light can mimic the effect of natural light and can consequently be used to entrain the circadian rhythm (Khalsa et al., 2003) and as such, if appropriately timed, can reduce circadian misalignment and provide better adaptation to a night work schedule (Smith et al., 2008).

In addition to circadian entrainment effects, light exposure can also elicit acute alerting responses, especially at night when alertness is normally low (Cajochen, 2007; Vandewalle et al., 2009; Souman et al., 2018). These nonvisual light responses have been shown to depend on several light characteristics (for a review see Prayag et al., 2019) including intensity (Cajochen et al., 2000; Zeitzer et al., 2000), exposure duration (Chang et al., 2012), and spectral distribution (Brainard et al., 2001; Thapan et al., 2001; Lockley et al., 2003; Cajochen et al., 2005; Lockley et al., 2006). In addition, there is individual variability in the responses to light exposure (Chellappa et al., 2017; Gabel et al., 2017; Phillips et al., 2019). Supported by classical rod and cone photoreceptors, the nonvisual light responses are mainly driven by intrinsically photosensitive retinal ganglion cells (ipRGCs), expressing the light-sensitive photopigment melanopsin, that project light information to the SCN and brain areas involved in sleep regulation, arousal, and attention (Perrin et al., 2004; Vandewalle et al., 2009; Warthen and Provencio, 2012). The power of light intensity in eliciting nonvisual responses such as alertness and circadian entrainment is well known (Cajochen et al., 2000; Zeitzer et al., 2000). However, as melanopsin is maximally sensitive to short-wavelength light around 460–490 nm (Bailes and Lucas, 2013), monochromatic blue and polychromatic blue-enriched light, especially at relatively low intensities, can also elicit larger nonvisual responses than light with longer wavelengths (Lockley et al., 2003; Cajochen et al., 2005; Lockley et al., 2006; Chellappa et al., 2011; Brainard et al., 2015).

Previous studies investigating nonvisual responses to nocturnal short-wavelength light have mainly been conducted in laboratory settings, applying monochromatic light, and carefully controlling the participants' environment, posture, nutritional intake and previous light exposure (Brainard et al., 2001; Thapan et al., 2001; Lockley et al., 2003; Cajochen et al., 2005; Lockley et al., 2006). Similarly, a few recent laboratory studies have included nocturnal polychromatic blue-enriched light (Cajochen et al., 2019; Hanifin et al., 2019). Thus, more naturalistic studies are warranted, and only a few recent studies have investigated nonvisual responses of nocturnal blue-enriched light during night work (Motamedzadeh et al., 2017; Sletten et al., 2017; Kazemi et al., 2018). Light conditions used in previous studies vary, and different ways of administering light such as by goggles, spheres and/or light boxes may not be applicable in practical settings. The development of cost-effective light emitting diode (LED) technology, has provided new and flexible strategies for illumination of workplaces (Schubert and Kim, 2005). Standard ceiling mounted LED-luminaires can easily be installed and tuned to provide light of specific intensity (Sunde et al., 2020), and/or specific spectral distributions (Canazei et al., 2017). Thus, LED-based standard lighting set-ups need to be investigated in order to elucidate if these light sources can sustain performance during night work. To the authors' knowledge, only two previous studies have investigated nonvisual responses to lighting administered by ceiling-mounted LEDs during simulated night work (Canazei et al., 2017; Sunde et al., 2020). In one previous study from our research group (Sunde et al., 2020), bright light (∼900 lx, 4000 K) improved alertness and performance compared to standard light (∼90 lx, 4000 K), while another study by Canazei et al. (2017) found that varied reduced portions of short-wavelength light (2166–4667 K, ∼150 lx) did not impact alertness and performance during night shifts.

In the present study (ClinicalTrials.gov: NCT03203538) we investigated how a standard LED-based polychromatic blue-enriched white light (7000 K; ∼200 lx), compared to warm white light (2500 K) of similar photon density (∼1.6×10^{14}

photons/cm^2/s), affected subjective alertness and performance on attention tests during three consecutive simulated night shifts, as well as circadian adaptation to the night work schedule. We also investigated participants' opinion of the lighting conditions and its feasibility for work. To ensure transferability to real-life settings, we employed relatively high illuminance (∼200 lx, at eye level in the direction of gaze) compliant with European standards for offices (CEN, 2011), as well as putting minimal restraints on participants during their spare time away from the laboratory night shifts. We hypothesized that three consecutive night shifts with 7000 K light would increase alertness and performance during shifts, and lead to a greater phase delay of the circadian rhythm hastening adaptation, compared to 2500 K light.

MATERIALS AND METHODS

Participants

All participants were between 19 and 30 years and reported good to excellent health; no current or recent history of psychiatric-, neurological-, cardiovascular-, lung-, and/or sleep diseases/disorders; no medication use (except contraceptives); no eye disease and no color deficiency according to the 17-plate Ishihara Test for Color Deficiency. Female participants were not pregnant or breastfeeding. Participants were not engaged in night work and had no transmeridian travel in the month prior to and/or during the study period and were not extreme chronotypes according to the short Morningness-Eveningness Questionnaire (Adan and Almirall, 1991). Participants reported habitual sleep duration of 6–10 h and habitual wake time between 06:00 and 10:00 h. Participants had to refrain from alcohol use for 3 days prior to and during the simulated night shifts; caffeine use 1 week prior to and during the night shifts; and tobacco use at least 2 h prior to and during the simulated night shifts.

Participants were mainly students invited via mass e-mail and flyers/information at the University of Bergen. Prior to enrolment participants were screened by an online survey to ensure that they were eligible. A total of 33 (10 males) pre-screened individuals attended an enrolment session at the laboratory 3 days prior to the first simulated night shift. Written informed consent was obtained before participants completed a set of questionnaires (demographics) and performed a practice sequence comprising a cognitive test battery (see section "Laboratory Procedure"). Participants were compensated for their participation. The study was conducted according to the Declaration of Helsinki.

Of the 33 enrolled participants, two withdrew before the first night shift and one participant was excluded from both study periods due to wake times after 10:00 h and/or sleep duration < 6 h during the three baseline sleep periods/nights at home (see section "Design and Procedure"). Three participants had their first study period excluded, one due to illness, and two due to wake times after 10:00 h during baseline sleep. The final data set comprised 30 (10 males) participants (**Table 1**) with 29 (9 males) completing the night shifts in 7000 K light, and 28 (8 males) completing the night shifts in 2500 K light. A total of 27 (7 males) participants had valid data included for all six night shifts.

TABLE 1 | Descriptive characteristics of the participants, and baseline sleep measured with actigraphy.

N total (males)	**30 (10)**	
Age [Mean (*SD*)]	23.3 (2.9)	
Body mass index [Mean (*SD*)]	23.2 (3.0)	
Self-reported health (%)		
Excellent	30.0	
Very good	53.0	
Good	17.0	
Short-MEQ (%)		
Moderately morning type	10.0	
Neither type	60.0	
Moderately evening type	30.0	
	7000 K light (*n* = 29) Mean (*SD*)	**2500 K light (*n* = 28) Mean (*SD*)**
Baseline sleep (hh:mm)		
Lights off	23:56 (1:11)	23:54 (0:57)
Sleep onset latency	0:17 (0:16)	0:14 (0:12)
Wake time	08:11 (0:55)	08:28 (1:15)
Time in bed	8:21 (1:10)	8:35 (1:18)

Short-MEQ, short Morningness-Eveningness Questionnaire. Baseline sleep: average for three nights prior to the first night shift (including one night with scheduled saliva sampling until 1 h after usual bedtime). There were no significant differences between the light conditions ($p > 0.05$).

Female participants reported their last menses onset and their usual menstrual cycle length. Using similar procedures as Vidafar et al. (2018), the menstrual phase (follicular, luteal) during the study periods was estimated. Three participants were in different menstrual phases during the two study periods, hence the vast majority (n = 17) were in the same menstrual phase during both study periods.

Design and Procedure

The study was conducted from January to April 2018 and included two study periods, separated by 4 weeks, each containing three consecutive simulated night shifts (23:00–06:45 h) performed during a weekend (Friday evening to Monday morning) in a laboratory (see **Figure 1**). The study was conducted at a latitude (∼60°N) and at a time of year with relatively limited daylight exposure in the hours before and after the night shifts. Participants were allocated into four groups of 7–9 participants, and a counterbalanced crossover design with repeated measurements was employed. Thus, each participant performed night shifts under both light conditions, with about half of the participants starting in the 7000 K light condition and the other half starting in the 2500 K light condition. Participants slept at home and were instructed to keep a regular sleep schedule prior to the first night shift in accordance with their habitual sleep timing. The baseline sleep 3 days prior to the first night shift (**Table 1**) was monitored by sleep diaries and actigraphy to ensure that participants did not "turn night into day" before starting the simulated night work period. Bedtime on Thursday evening was not habitual due to hourly saliva sampling for estimation of dim-light melatonin onset (DLMO), which lasted until 1 h

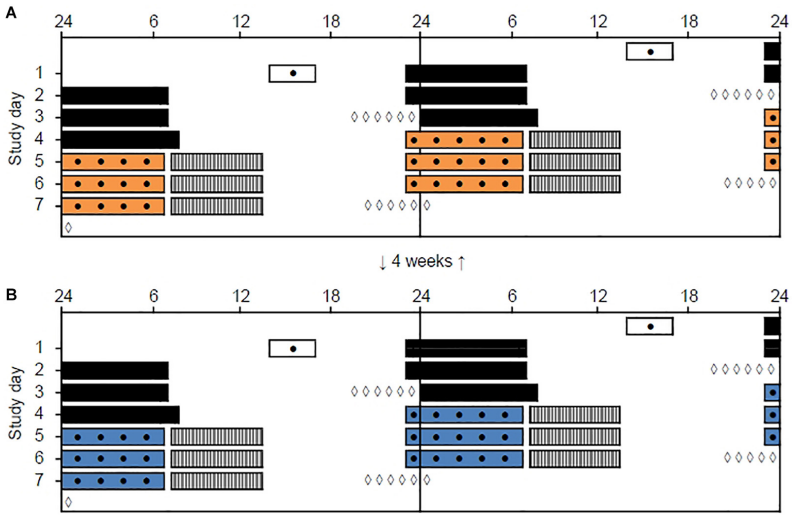

FIGURE 1 | Double-raster plot of the simulated night work protocol. Clock hour is indicated on the *x*-axis and study day on the *y*-axis. The night work protocol included two study periods with three simulated night shifts (from 23:00 to 06:45 h) performed in a laboratory with different lighting conditions. **(A)** 2500 K light. **(B)** 7000 K light. The study periods were separated by 4 weeks and the order of conditions was counterbalanced. White bars indicate enrollment and practice session (before the first study period only) in the laboratory. Black bars indicate assumed baseline sleep at home. Colored bars indicate night shifts in the laboratory. Gray hatched bars indicate assumed daytime sleep at home. Black dots indicate primary test bouts including the Karolinska Sleepiness Scale (KSS), a Psychomotor Vigilance Task (PVT), and a Digit Symbol Substitution Test (DSST). White diamonds indicate salivary dim-light melatonin sampling at home.

after usual bedtime. Napping was allowed before the night shifts, but not after 20:00 h and/or longer than 2 h. After completing the night shift in the laboratory participants went home to sleep *ad libitum* and with no restrictions concerning other activities, before meeting at the laboratory to complete the next night shift.

Sleep diaries and actigraphy indicated that napping was similar across study conditions. In 7000 K light, 18, 12, and 8 participants napped prior to the first, second, and third night shift, respectively. In 2500 K light, 14, 12, and 11 participants napped prior to the first, second, and third night shift, respectively. The duration of napping across conditions was also similar, with an overall mean napping duration of 1:14 (*SD* = 0:36) h and 1:21 (*SD* = 0:41) h in 7000 and 2500 K light, respectively. Most participants' napping behavior was consistent for both study periods, and in terms of differences in napping between the light conditions, counterbalancing ensured that napping was very similar for both light conditions.

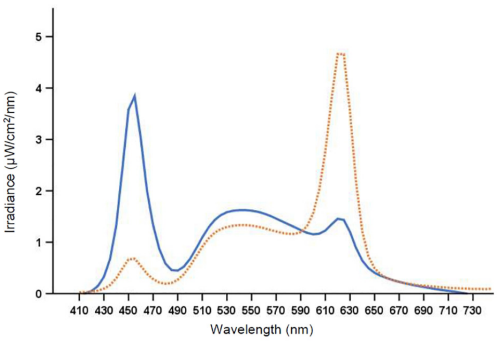

FIGURE 2 | Spectral distribution of the 7000 K light (solid line) and the 2500 K light (dotted line).

Laboratory and Light Exposure

The laboratory (30 m^2) had no windows and the temperature was kept constant at ∼22°C. There were nine workplaces, each separated by partition walls, with identical desktop computers and screens fitted with a filter (Metolight SFG-10; Asmetec, Germany) blocking all light wavelengths < 520 nm. The laboratory was equipped with 20 ceiling mounted LED-luminaires (Modul R 600 LED CCT/RGB MP; Glamox Luxo Lighting AB, Sweden). Participants were exposed to polychromatic full-spectrum light with a color temperature of ∼7000 and ∼2500 K, respectively. The photopic illuminance was ∼200 lx in the vertical plane at eye level (∼600 lx in the horizontal plane), with similar photon density (∼1.6 × 10^{14} photons/cm^2/s) for both light conditions. The color rendering index (R_a) was > 80, and both light conditions were compliant with European standards for most interior areas, e.g., offices (CEN, 2011). **Figure 2** shows the average spectral distribution of

the light conditions measured at each workplace in the vertical plane, at eye level while seated (120 cm from the floor), using a spectroradiometer (GL Spectis 1.0 T Flicker; GL Optic, Poland). The photometric information of the light conditions is reported in **Table 2**, estimated using the Lucas et al. (2014) toolbox.

Laboratory Procedure

The simulated night shifts started at 23:00 h with a 30 min preparation and adaptation period in the laboratory. At 23:30 h the first of five repeated main test bouts (23:30, 01:00, 02:30, 04:00, and 05:30 h) commenced. Each test bout lasted ∼20 min and included the Karolinska Sleepiness Scale (KSS) (Åkerstedt and Gillberg, 1990), a computerized Psychomotor Vigilance Task (PVT) (Dinges and Powell, 1985), and a computerized Digit Symbol Substitution Test (DSST) (Jaeger, 2018). During testing participants were seated at their designated workplace and wore noise canceling headsets (BOSE QuietComfort 25, BOSE Corporation, United States) to ensure undisturbed performance. Between the main test bouts participants performed other tests and had breaks allowing quiet activities such as reading and conversation. A researcher was present throughout the night shifts to ensure adherence to the protocol. Water was available *ad libitum* during the night shift, and at about 02:00 h and 05:00 h a small standardized meal/snack (∼200 kcal) was provided.

Alertness and Performance Measures

The KSS assesses subjective alertness/sleepiness (Åkerstedt and Gillberg, 1990), and was completed at the beginning and end of each test bout with participants indicating their current level of sleepiness on a 9-point Likert scale ranging from 1, "very alert," to 9, "very sleepy, fighting sleep, strenuous to keep awake." We analyzed the average KSS rating for each test bout as a measure of the participants' subjective alertness level.

The PVT assesses the ability to sustain attention and is a sensitive measure for detecting sleep loss and sleep deprivation effects (Lim and Dinges, 2008; Basner and Dinges, 2011). The PVT shows minor aptitude and learning effects and is thus suitable for repeated administration (Lim and Dinges, 2008). A 10 min version was used in the present study, and participants were instructed to respond with their dominant hand on the space bar when presented with a visual stimulus (a counting timer) on the screen. The interstimulus interval varied randomly from 2 to 10 s including 1 s feedback on response time (RT) after each trial. If no response was given after 30 s, a sound was played to alert the participant before a new trial began. RTs < 100 ms was considered false starts. The mean number of trials per PVT was 95 ($SD = 6$). The primary outcome metrics comprised the mean 1/RT (reciprocal RTs) and the number of lapses (RTs ≥ 500 ms) as suggested by Basner and Dinges (2011), but also the number of false starts (responses without stimulus), the fastest 10% RT (mean RT for the 10% fastest responses) and the slowest 10% 1/RT (mean 1/RT for the 10% slowest responses) were reported.

The DSST was administered directly following the PVT and provided a second performance measure sensitive to changes in cognitive function (Jaeger, 2018). Performance on the DSST improves with repeated administrations (Jaeger, 2018). To minimize these learning effects participants practiced the DSST once during the enrollment session 3 days prior to the first night shift, and the symbol-digit pairs were randomized for each administration. A 2 min version was used, and participants were instructed to pair nine randomly presented symbols with their corresponding digit as fast as possible without making errors. Target symbols were presented at the center of the screen and participants selected the corresponding digit from a symbol-digit array, displayed at the bottom of the screen continuously during the test. Participants used the mouse pointer to select the digits, and if no response was recorded after 5 sec, the next trial began. The mean number of trials per DSST was 81 ($SD = 9$), and the number of correct responses was used as the outcome metric.

TABLE 2 | Lighting parameters (380–780 nm inclusive) for nine workplaces.

	7000 K light Mean (*SD*)	2500 K light Mean (*SD*)
Correlated color temperature (K)	6953 (260)	2455 (43)***
Irradiance ($\mu W/cm^2$)	61 (6)	55 (5)*
Photon flux (photons/cm^2/s)	1.65×10^{14} (1.55×10^{13})	1.61×10^{14} (1.37×10^{13})
Photopic illuminance (lx)	197 (19)	206 (18)
Human retinal photopigment weighted illuminance (α-opic lx)		
Cyanopic	220 (23)	40 (4)***
Melanopic	192 (19)	86 (8)***
Rhodopic	195 (19)	113 (11)***
Chloropic	196 (19)	160 (54)***
Erythropic	190 (18)	206 (18)

*Light measured 120 cm from the floor in the vertical plane. Values calculated according to the Lucas et al. (2014) toolbox. *$p < 0.05$; ***$p < 0.001$, compared to 7000 K light.*

Circadian Phase and Sleep

To provide a measure of circadian phase before and after each night work period, we assessed salivary DLMO on Thursday evening ("baseline DLMO") and Monday evening ("final DLMO"). Hourly saliva sampling (six samples) was performed at home, using Salivette tubes (Sarstedt AG & CO, Germany), following a similar protocol previously described (Saxvig et al., 2013). Baseline DLMO sampling started 4 h before and lasted until 1 h after participants' habitual bedtime, while final DLMO sampling was delayed by 1 h relative to the baseline DLMO sampling (**Figure 1**). To ensure dim light during sampling, participants were instructed to wear dark sunglasses (Uvex Athletic ISO 9001, Uvex Winter Holding GmbH & Co. KG, Germany) from 1 h prior to, and during, the whole sampling period. The lenses of these glasses reduce light intensity to <1.0% (Saxvig et al., 2013). Participants labeled the samples with clock time and stored them in their domestic refrigerator before delivery at the laboratory for storage at – 70°C.

Samples were assayed with enzyme-linked immunosorbent assay kit (EK-DSM, Bühlman Laboratories, Switzerland). The detection limit of the assay kit is 0.5 pg/mL and the functional sensitivity is 1.6–20.5 pg/mL. Samples were analyzed using a Wallac 1420 Multilabel counter (Perkin Elmer Inc., United States). The inter-assay variation was 13.4% for the low

and 12.3% for the high control, with mean (*SD*) melatonin values of 5.3 (0.7) and 15.5 (1.9) pg/mL, respectively. The DLMO was defined as the time salivary melatonin concentration reached 4 pg/mL. Linear interpolation between adjacent samples was used to calculate DLMO, and if levels reached 3 pg/mL but not 4 pg/mL linear extrapolation was used (Keijzer et al., 2011). The difference between baseline DLMO and final DLMO was calculated to estimate the magnitude of the circadian phase shift after the three consecutive night shifts. In accordance with previously reported procedures (Smith et al., 2008), we also estimated the temperature minimum (Tmin) for each participant by adding 7 h to the DLMO. The phase angle after the night shifts was estimated based on the final DLMO and sleep onset and sleep offset of the daytime sleep after the third night shift. We excluded one participant's phase angle for sleep onset, and one participant's phase angle for sleep offset, due to social commitments interfering with the daytime sleep after the third night shift.

The circadian phase shift could only be calculated for a subset of the participants due to missing DLMO data. For 7000 K light, phase shifts were estimated for 20 (69.0%) of the 29 included participants, and for 2500 K light phase shifts were estimated for 22 (78.6%) of the 28 included participants. Five (16.7%) of the 30 participants had no valid phase shift estimates, while complete phase shift estimates (for both light conditions) were available for 17 (56.7%) participants. The main reason for missing DLMO data was that salivary melatonin concentration did not reach 3 pg/mL during DLMO sampling. For 7000 K light, two (6.9%) and six (20.7%) participants did not reach 3 pg/mL during baseline and final DLMO sampling, respectively. For 2500 K light, one (3.6%) and three (10.7%) participants did not reach 3 pg/mL during baseline and final DLMO sampling, respectively.

Sleep data were derived from wrist actigraphy (Actiwatch 2, Philips Respironics Inc., United States), worn on the non-dominant hand. Data were recorded in 30 s epochs with medium wake threshold sensitivity (40 counts/min), and time of inactivity for sleep onset and wake time set to 10 min (Actiware version 6.0, Phillips Respironics Inc., United States). As recommended (Smith et al., 2018), the start and end of rest intervals were manually scored based on a standardized inspection of the raw data and sleep diaries.

Evaluation of Lighting Conditions

To assess participants' subjective evaluation of the lighting conditions, a questionnaire comprising a semantic differential scale adapted from Smolders and de Kort (2014, 2017) was used. The scale consists of nine adjective items on a 7-point scale. The first four items comprised the subscale "pleasantness" of the lighting ("unpleasant–pleasant," "uncomfortable–comfortable," "disturbing–not disturbing," and "causing glare–not causing glare") which was internally reliable with Cronbach's $\alpha = 0.82$, similar to that reported by Smolders and de Kort (2014, 2017). Four single items were used to assess the "clearness" ("unclear–clear"), "color" ("warm–cold"), "brightness" ("dim–bright"), and if the lighting was "activating" ("relaxing–stimulating"). One item was used to assess if the lighting was "suitable for work" ("unsuitable for work–suitable for work"). The evaluation of lighting conditions was completed at the beginning (∼23:15 h) of the first night shift and at the end (∼06:15 h) of the third night shift in both light conditions.

Statistical Analysis

To analyze the KSS, PVT mean 1/RT, fastest 10% RT, slowest 10% 1/RT and DSST we used linear mixed models (LMM). Three LMMs for each of the dependent variables were modeled. In a random effect model *participant* was included as a random effect. In a main effects model, *light* (7000 K vs. 2500 K), *shift* (night 1, night 2, and night 3) and *time* (23:30, 01:00, 02:30, 04:00, and 05:30 h) were entered as fixed factors. In the interaction effects model *light* × *shift*, *light* × *time*, *shift* × *time,* and *light* × *shift* × *time* were entered. *Time* was treated as a fixed factor due to the fixed timing of the main test bouts, and that there were some protocol differences in tasks and occurrences between the test bouts (e.g., provision of a standardized snack). The LMMs were run with a maximum likelihood estimation, enabling comparison of the fit of successive models using -2 times the log of the likelihood (-2LL) to conduct a likelihood ratio test (*LRT*). The difference in -2LL between the random effect model and the main effects model, and between the main effects model and the interaction effects model was compared to the chi-square distribution. The degrees of freedom (*df*; with Satterthwaite approximation) used for comparison were equal to the difference in the number of parameters between the compared models. If there were significant interaction effects, but the *LRT* indicated poorer model fit, we trimmed the interaction effects model by removing non-significant interaction effects before conducting a second *LRT*, comparing the main effects model and the trimmed interaction effects model. The residuals from the final LMM were tested for normality with Shapiro-Wilk tests and by assessment of normality plots to ensure that assumptions were met. *F*-statistics are reported and pseudo R^2 statistics (reduction in variance given as: % explained variance) were calculated for the models with the best fit. Multiple comparisons were performed using Bonferroni corrections to evaluate the difference between light conditions, shifts and time points. To visualize the findings for the KSS, PVT mean 1/RT and the DSST, we plotted the estimated marginal means (*EMM*) and the standard errors (*SE*) for the *light* × *shift* × *time* interaction, although the interaction effects model did not have the best fit. The PVT fastest 10% RT and slowest 10% 1/RT were plotted as a function of *light* and *time*, as the trimmed interaction effects model including the *light* × *time* interaction had the best model fit for the fastest 10% RT.

The number of PVT lapses and false starts were analyzed using generalized linear mixed models (GLMM) with a negative binominal distribution, as features of these count variables showed overdispersion and a distribution skewed toward zero. A corresponding modeling approach as described for the LMM (random effect model, main effects model and interaction effects model) was used for the GLMM. We employed Satterthwaite approximation for the *df* and robust estimation of standard errors (*SE*). The GLMM analyses use restricted maximum likelihood estimation, thus the *LRT* approach for testing model fit is not appropriate for comparing these models. The Akaike's information criterion (*AIC*) and the Schwarz's Bayesian criterion

(*BIC*) were instead used for comparison of models (the model with the smallest *AIC*/*BIC* values was preferred).

To assess the effect of light condition on the magnitude of the circadian phase shift, we used an LMM with *participant* included as a random effect and *light* entered as a fixed factor. We used similar settings as described for the previous analyses and comparison with Bonferroni adjustments were made to evaluate the difference in effect between light conditions. Initial differences in baseline DLMO between the light conditions were investigated by paired samples *t*-tests. The difference in baseline DLMO was also investigated including only participants with complete DLMO estimates ($n = 17$) in both light conditions. To assess if baseline DLMO correlated with phase shift magnitude, we calculated Pearson's product-moment correlation coefficients. We also assessed, using *t*-tests, the differences between light conditions for the baseline sleep and phase angle variables. Daytime sleep after the night shifts was analyzed with LMMs using similar procedures as described previously. *Participant* was included as a random effect and *light*, *shift*, and the *light* × *shift* interaction were entered as fixed factors.

To analyze the evaluation of light conditions, LMMs were used in a similar modeling approach (and settings) as described above. For each of the six dependent variables (pleasantness, clearness, color, brightness, activating, and work suitability), a random effect model with *participant* included as a random effect; a main effects model with *light* entered as a fixed factor; and a time-interaction effects model with *time* [time 1 (start of first shift) vs. time 2 (end of last shift)] and the *light* × *time* interaction entered as fixed factors were computed. *LRT*s were used to assess model fit (random to main effects model; $df = 1$, main to time-interaction effects model; $df = 2$), and multiple comparisons with Bonferroni corrections were conducted to investigate the difference between light conditions.

All statistical analysis was performed using IBM SPSS Statistics, version 25 (IBM Corp., United States).

RESULTS

Karolinska Sleepiness Scale (KSS)

For KSS (**Table 3**) there were significant main effects of *light* with reduced sleepiness/increased alertness in 7000 K compared to 2500 K light; *shift* with increased alertness on night 2 ($EMM = 6.29$; $SE = 0.16$, $p = 0.003$) and night 3 ($EMM = 5.84$; $SE = 0.16$, $p < 0.001$) compared to night 1 ($EMM = 6.59$; $SE = 0.16$); and *time* with reduced alertness at 01:00 ($EMM = 5.71$; $SE = 0.17$, $p < 0.001$), 02:30 ($EMM = 6.05$; $SE = 0.17$, $p < 0.001$), 04:00 ($EMM = 6.99$; $SE = 0.17$, $p < 0.001$) and 05:30 h ($EMM = 7.50$; $SE = 0.17$, $p < 0.001$) compared to 23:30 h ($EMM = 4.95$; $SE = 0.17$). The main effects model had the best fit ($df = 7$, $LRT = 462.53$) and explained 32.3% of the variance in KSS scores. There were no significant interaction effects (**Figure 3A**).

Psychomotor Vigilance Task (PVT)

For mean 1/RT (**Table 3**) there were no significant main effects of *light* or *shift*, but there was a significant main effect of *time* with slower RTs at 01:00 ($EMM = 3.14$; $SE = 0.08$, $p < 0.001$), 02:30 ($EMM = 3.04$; $SE = 0.08$, $p < 0.001$), 04:00 ($EMM = 2.91$; $SE = 0.08$, $p < 0.001$) and 05:30 h ($EMM = 2.78$; $SE = 0.08$, $p < 0.001$) compared to 23:30 h ($EMM = 3.31$; $SE = 0.08$). The main effects model had the best model fit ($df = 7$, $LRT = 218.68$) and explained 9.9% of the variance in mean 1/RT. There were no significant interaction effects (**Figure 3B**).

For number of lapses (**Table 3**) there were no significant main effects of *light* or *shift*, but there was a significant main effect of *time* with more lapses at 01:00 ($EMM = 3.37$; $SE = 0.73$, $p < 0.001$), 02:30 ($EMM = 4.84$; $SE = 1.07$, $p < 0.001$), 04:00 ($EMM = 7.32$; $SE = 1.31$, $p < 0.001$) and 05:30 h ($EMM = 9.84$; $SE = 1.79$, $p < 0.001$) compared to 23:30 h ($EMM = 1.79$; $SE = 0.40$). There were also significant interaction effects of *shift* × *time* with fewer lapses at 04:00 ($EMM = 5.92$; $SE = 1.31$, $p = 0.005$) and 05:30 h ($EMM = 7.05$; $SE = 1.53$, $p = 0.001$) on night 3 compared to 04:00 h ($EMM = 8.53$; $SE = 1.39$) and 05:30 h ($EMM = 12.35$; $SE = 2.15$) on night 1; and *light* × *shift* × *time* (**Figure 3C**). The interaction effects model (*AIC, BIC* = 2717, 2722) had smaller *AIC/BIC* values than the main (*AIC, BIC* = 2741, 2746) and random (*AIC, BIC* = 2819, 2824) effects model.

For number of false starts (**Table 3**) there were no significant main effects of *light* or *shift*, but there was a significant main effect of *time* with more false starts at 05:30 h ($EMM = 4.01$; $SE = 0.657$, $p = 0.001$) compared to 23:30 h ($EMM = 1.66$; $SE = 0.26$). There were also significant interaction effects of *light* × *time* with fewer false starts at 05:30 h with 7000 K ($EMM = 3.33$; $SE = 0.57$, $p = 0.040$) compared to 2500 K ($EMM = 4.83$; $SE = 0.93$) light; and *light* × *shift* × *time* (**Figure 3D**). The interaction effects model (*AIC, BIC* = 2636, 2641) had smaller *AIC/BIC* values than the main (*AIC, BIC* = 2676, 2681) and random (*AIC, BIC* = 2880, 2884) effects model.

On the fastest 10% RT (**Table 3**) there was no significant main effect of *light*, but there were significant main effects of *shift* with shorter RTs on night 2 ($EMM = 258.08$; $SE = 4.61$, $p < 0.022$) and night 3 ($EMM = 256.18$; $SE = 4.61$, $p < 0.001$) compared to night 1 ($EMM = 261.58$; $SE = 4.61$); and *time* with longer RTs at 01:00 ($EMM = 255.60$; $SE = 4.67$, $p < 0.001$), 02:30 ($EMM = 258.45$; $SE = 4.67$, $p < 0.001$), 04:00 ($EMM = 264.69$; $SE = 4.67$, $p < 0.001$) and 05:30 h ($EMM = 267.33$; $SE = 4.67$, $p < 0.001$) compared to 23:30 h ($EMM = 247.00$; $SE = 4.67$). There was a significant interaction effect of *light* × *time* (**Figure 4A**). The trimmed interaction effects model, including the *light* × *time* interaction, had a better model fit than the main effects model ($df = 4$, $LRT = 11.56$) and explained 6.0% of the variance in the fastest 10% RT.

On the slowest 10% 1/RT (**Table 3**) there were no significant main effects of *light* or *shift*, but there was a significant main effect of *time* with longer RTs at 01:00 ($EMM = 2.05$; $SE = 0.09$, $p < 0.001$), 02:30 ($EMM = 1.89$; $SE = 0.09$, $p < 0.001$), 04:00 ($EMM = 1.71$; $SE = 0.09$, $p < 0.001$) and 05:30 h ($EMM = 1.51$; $SE = 0.09$, $p < 0.001$) compared to 23:30 h ($EMM = 2.29$; $SE = 0.09$). The main effects model had the best model fit ($df = 7$, $LRT = 217.73$) and explained 13.2% of the variance in the slowest 10% 1/RT. There were no significant interaction effects (**Figure 4B**).

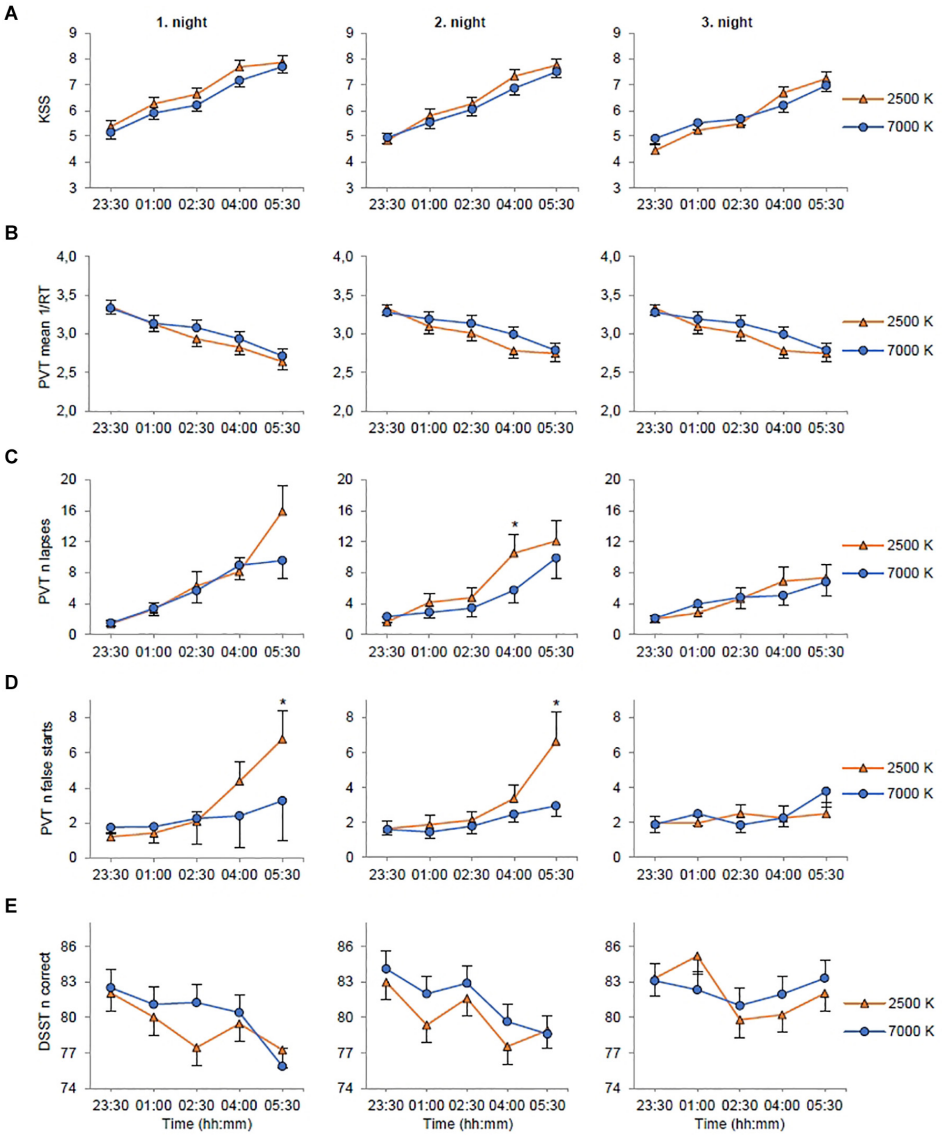

FIGURE 3 | Estimated marginal means and standard error plotted as a function of light condition (2500 K vs. 7000 K light), night shift, and time of testing. **(A)** Rating on the Karolinska Sleepiness Scale (KSS). **(B)** Mean reciprocal response time (1/RT) on the Psychomotor Vigilance Task (PVT). **(C)** Number of lapses (RTs ≥ 500 ms) on the PVT. **(D)** Number of false starts (response without stimulus) on the PVT. **(E)** Number of correct responses on the Digit Symbol Substitution Test (DSST). *$p < 0.05$ between light conditions (only for variables with significant *light* × *night* × *time* interactions).

Digit Symbol Substitution Test (DSST)

For the number of correct responses on the DSST (**Table 3**) there were significant main effects of *light* with more correct responses in 7000 K compared to 2500 K light; *shift* with more correct responses on night 3 ($EMM = 82.24$; $SE = 1.15$, $p < 0.001$) compared to night 1 ($EMM = 79.74$; $SE = 1.15$); and *time* with fewer correct responses at 02:30 ($EMM = 80.67$; $SE = 1.18$, $p < 0.001$), 04:00 ($EMM = 79.89$; $SE = 1.18$, $p < 0.001$) and

TABLE 3 | Alertness and performance estimates for the light conditions, and *F*-statistics for fixed factors.

	7000 K light	2500 K light	Light		Shift		Time		Light*Shift		Light*Time		Shift*Time		Light*Shift*Time	
	EMM (SE)	*EMM (SE)*	*F (df)*	*p*	*F (df)*	*p*	*F (df)*	*p*	*F (df)*	*p*	*F (df)*	*p*	*F (df)*	*p*	*F (df)*	*p*
KSS [1-9 (sleepy)]	6.15 (0.16)	6.32 (0.16)	**4.58 (1.834)**	**0.033**	**31.80 (2.825)**	**<0.001**	**138.05 (4.825)**	**<0.001**	2.10 (2.825)	0.123	1.63 (4.825)	0.165	0.54 (8.825)	0.824	0.47 (8.825)	0.892
PVT mean 1/RT	3.06 (0.08)	3.01 (0.08)	2.89 (1.812)	0.090	1.64 (2.807)	0.195	**61.25 (4.807)**	**<0.001**	2.15 (2.807)	0.117	1.71 (4.807)	0.146	1.57 (8.807)	0.129	0.38 (8.807)	0.931
PVT *n* lapses	4.39 (0.93)	4.86 (0.96)	0.42 (1.807)	0.519	1.54 (2.807)	0.214	**27.08 (4.807)**	**<0.001**	0.59 (2.807)	0.555	9.99 (4.807)	0.999	**3.48 (8.807)**	**0.001**	**2.95 (8.807)**	**0.003**
PVT *n* false starts	2.19 (0.34)	2.49 (0.41)	1.53 (1.807)	0.308	0.08 (2.807)	0.921	**10.48 (4.807)**	**<0.001**	2.40 (2.807)	0.092	**2.61 (4.807)**	**0.034**	1.73 (8.807)	0.089	**2.78 (8.807)**	**0.005**
PVT fastest 10% RT	257.99 (4.57)	259.24 (4.58)	1.52 (1.810)	0.283	**7.95 (2.807)**	**<0.001**	**40.80 (2.807)**	**<0.001**	0.21 (2.807)	0.812	**2.91 (4.807)**	**0.021**	1.02 (8.807)	0.421	0.55 (8.807)	0.821
PVT slowest 10% 1/RT	1.92 (0.09)	1.86 (0.09)	2.65 (1.815)	0.104	1.08 (2.807)	0.339	**61.29 (4.807)**	**<0.001**	2.64 (2.807)	0.072	0.79 (4.807)	0.534	1.64 (8.807)	0.110	0.62 (8.807)	0.760
DSST *n* correct	81.35 (1.14)	80.50 (1.14)	**4.82 (1.816)**	**0.028**	**14.83 (2.810)**	**<0.001**	**12.20 (4.810)**	**<0.001**	0.80 (2.810)	0.449	1.26 (4.810)	0.285	**4.37 (8.810)**	**<0.001**	1.30 (8.810)	0.239

EMM, estimated marginal means. SE, standard error. KSS, Karolinska Sleepiness Scale. PVT, Psychomotor Vigilance Task. DSST, Digit Symbol Substitution Test. Estimates and statistics were calculated using linear- or generalized linear mixed models. Significant findings are indicated in bold.

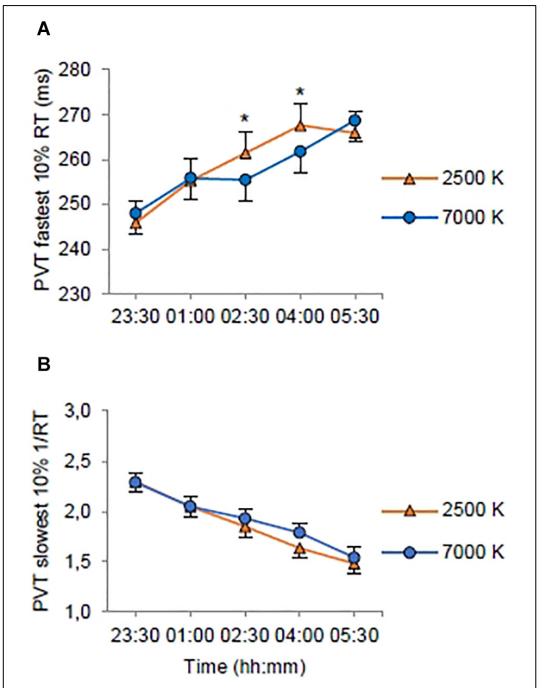

FIGURE 4 | Estimated marginal means and standard error plotted as a function of light condition (2500 K vs. 7000 K light) and time of testing (all night shifts included). **(A)** Response times (RT) for the 10% fastest RTs on the Psychomotor Vigilance Task (PVT). **(B)** Mean resiprocal RTs (1/RT) for the 10% slowest RTs on the PVT. *$p < 0.05$ between light conditions.

05:30 h (*EMM* = 79.33; *SE* = 1.18, $p < 0.001$) compared to 23:30 h (*EMM* = 83.02; *SE* = 1.18). There was also a significant interaction effect of *shift*× *time* with more correct responses at 02:30 h on night 2 (*EMM* = 82.26; *SE* = 1.32, $p = 0.015$) compared to night 1 (*EMM* = 79.36; *SE* = 1.32), at 01:00 h on night 3 (*EMM* = 83.78; *SE* = 1.32, $p = 0.006$) compared to night 1 (*EMM* = 80.57; *SE* = 1.32) and at 05:30 h on night 3 (*EMM* = 82.69; *SE* = 1.32, $p < 0.001$) compared to night 1 (*EMM* = 76.56; *SE* = 1.32). There were fewer correct responses at 02:30 (*EMM* = 79.36; *SE* = 1.32, $p < 0.045$) and 05:30 h (*EMM* = 76.56; *SE* = 1.32, $p < 0.001$) compared to 23:30 h (*EMM* = 82.29; *SE* = 1.32) on night 1, and at 04:00 (*EMM* = 78.60; *SE* = 1.32, $p < 0.001$) and 05:30 h (*EMM* = 78.75; *SE* = 1.32, $p < 0.001$) compared to 23:30 h (*EMM* = 83.55; *SE* = 1.32) on night 2. The interaction effects model had the best model fit (*df* = 22, *LRT* = 50.43) and explained 6.2% of the variance in the number of correct responses. However, there were no significant interaction effects of *light* × *time* or *light* × *shift* × *time* (**Figure 3E**).

Circadian Phase and Sleep

All participants, except one in each light condition, showed a relatively robust circadian phase delay (≥30 min) after working

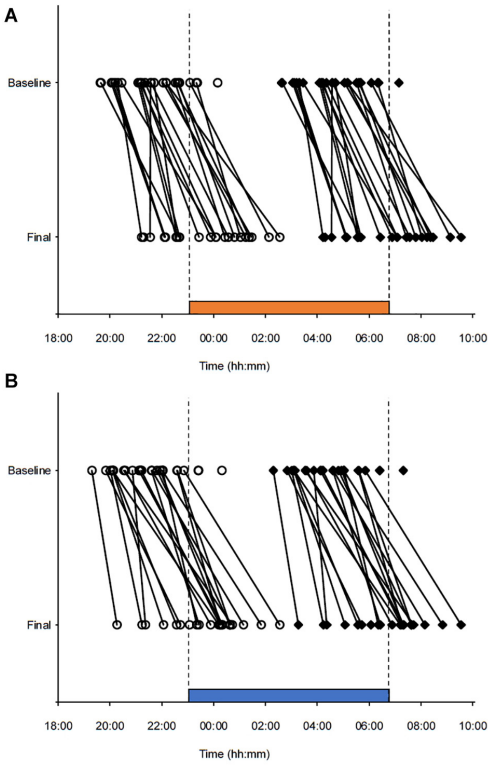

FIGURE 5 | Phase markers for individual participants before (baseline) and after (final) three consecutive night shifts. **(A)** Night shifts in 2500 K light. **(B)** Night shifts in 7000 K light. Open circles indicate salivary dim-light melatonin onset (DLMO) for each participant. Filled diamond squares indicate estimated temperature minimum (DLMO + 7 h) for each participant. Lines are drawn between the baseline and final markers for each participant with complete baseline and final markers. The vertical dotted lines and the horizontal bars indicates the start and end times of the night shifts and light exposure.

three consecutive night shifts (**Figure 5**). For 7000 K light, the baseline DLMO (n = 26) ranged from 19:18 to 00:19 h, and for the final DLMO (n = 22) the range was 20:16–02:33 h. For 2500 K light, the baseline DLMO (n = 26) ranged from 19:37 to 00:09 h, and for the final DLMO (n = 23) the range was 21:13–02:33 h. In **Table 4**, DLMO and sleep statistics are provided for participants with complete data. Eleven participants had a larger phase delay after night shifts in 7000 K than in 2500 K light, while six participants showed an opposite effect. The LMM estimated mean phase delay of DLMO was 2:34 (SE = 0:14) h and 2:12 (SE = 0:14) h in the 7000 and 2500 K light conditions, respectively. However, there was no significant main effect of *light* ($F_{1,23}$ = 1.58; p = 0.222). There was no significant difference in the initial timing of baseline DLMO before the night shifts

TABLE 4 | Daytime sleep and circadian phase markers. Clock time (hh:mm).

	n	7000 K light Mean (*SD*)	2500 K light Mean (*SD*)
Daytime sleep			
Sleep onset	27	07:45 (0:28)	07:45 (0:32)
Sleep onset latency	27	0:06 (0:06)	0:05 (0:06)
Wake time	27	13:47 (0:57)	13:28 (1:00)
Sleep duration	27	6:01 (0:57)	5:43 (0:58)
Circadian phase			
Baseline DLMO	23	21:27 (1:10)	21:30 (1:06)
Final DLMO	18	23:54 (1:23)	23:36 (1:31)
Phase shift (delay)	17	2:43 (1:04)	2:12 (1:14)
Phase angle			
Phase angle sleep onset	16	7:36 (1:07)	7:47 (1:27)
Phase angle sleep offset	16	13:37 (2:35)	13:38 (1:55)

Participants with complete data for each variable. Sleep variables derived from averaged actigraphy of the three daytime sleep periods after the night shifts. DLMO, dim-light melatonin onset. Baseline DLMO sampled in the evening one day prior to the first night shift; Final DLMO sampled in the evening on the day after the third night shift. Phase angle calculated as the time interval from final DLMO to sleep onset and offset, derived from actigraphy of the previous daytime sleep period (after the third night shift). There were no significant differences between the light conditions ($p > 0.05$).

across the two conditions (**Table 4**). Similar results were found when analyzing baseline DLMO for the 17 participants who had complete DLMO estimates in both light conditions (7000 K: M = 21:13; SD = 0:55, 2500 K: M = 21:27; SD = 1:03, t_{16} = 1.21; p = 0.243). The magnitude of phase shift and baseline DLMO did not correlate in either of the conditions (7000 K: r = 0.111; p = 0.640, 2500 K: r = 0.108; p = 0.632).

Participants had a mean daytime sleep duration after night shifts of 6:01 h in 7000 K light and 5:43 h in 2500 K light, which did not amount to a significant difference. Likewise, for the other daytime sleep variables, there were no significant differences between light conditions (**Table 4**). Also, the phase angle relationship for sleep onset and sleep offset did not differ significantly between the light conditions. In **Figures 6A–D**, estimates of daytime sleep after each night shift are provided. There was no significant main effect of *light* nor an interaction effect of *light* × *shift* for any of the sleep variables, and for sleep onset latency and wake time there were no significant effect of any of the fixed factors. For sleep onset there was a main effect of *shift* [$F_{(2,\ 139)}$ = 6.14; p = 0.003] with later sleep onset for daytime sleep after night 3 (EMM = 08:01 h; SE = 0:06 h) compared to daytime sleep after night 1 (EMM = 07:40 h; SE = 0:06 h, p = 0.013) and night 2 (EMM = 07:38 h; SE = 0:06 h, p = 0.006). The main effects model explained 5.5% of the variance in sleep onset. For sleep duration there was a main effect of *shift* [$F_{(2,\ 139)}$ = 8.23; $p < 0.001$] with shorter sleep duration for daytime sleep after night 3 (EMM = 5:31 h; SE = 0:12 h) compared to daytime sleep after night 1 (EMM = 6:03 h; SE = 0:12 h, p = 0.046) and night 2 (EMM = 6:24 h; SE = 0:12 h, $p < 0.001$). The main effects model explained 8.1% of the variance in sleep duration.

Light Evaluation

For all the light evaluation items there was a significant main effect of *light* (**Table 5**). Participants evaluated 2500 K as more

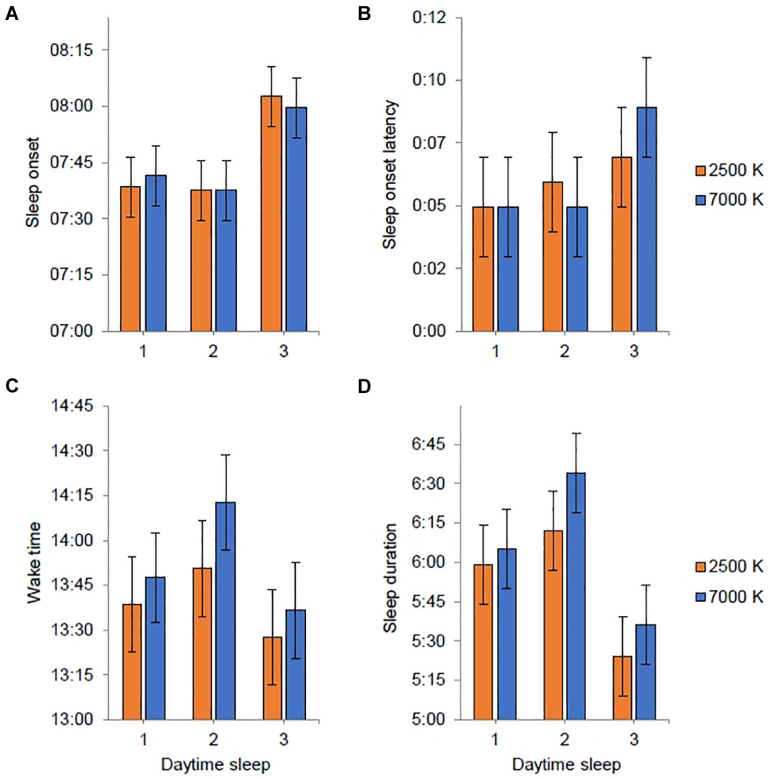

FIGURE 6 | Estimated marginal means and standard error plotted as a function of light condition (2500 K vs. 7000 K light) and daytime sleep period (after night shift 1–3). Sleep variables were derived from actigraphy. Estimates are provided as clock time (hh:mm) for **(A,C)** and duration (h:mm) for **(B,D)**. No statistically significant differences between light conditions were found.

TABLE 5 | Evaluation of light conditions estimates, and *F*-statistics for fixed factors.

	7000 K light	2500 K light	*Light*		*Time*		*Light*Time*		Variance (%) explained by *light*
	EMM (SE)	*EMM (SE)*	*F (df)*	*p*	*F (df)*	*p*	*F (df)*	*p*	
Pleasantness	4.64 (0.17)	5.13 (0.17)	**5.27 (1.88)**	**0.024**	0.13 (1.85)	0.725	**5.29 (1.85)**	**0.024**	**3.9**
Clearness	5.51 (0.23)	3.95 (0.23)	**41.27 (1.85)**	**<0.001**	0.21 (1.83)	0.651	1.08 (1.83)	0.301	**18.5**
Color	5.62 (0.22)	3.08 (0.22)	**75.19 (1.86)**	**<0.001**	1.58 (1.82)	0.213	0.41 (1.82)	0.525	**38.3**
Brightness	4.73 (0.19)	3.67 (0.19)	**29.10 (1.81)**	**<0.001**	1.82 (1.79)	0.181	0.49 (1.79)	0.484	**13.4**
Activating	5.11 (0.22)	3.24 (0.22)	**60.90 (1.84)**	**<0.001**	1.21 (1.82)	0.275	2.94 (1.82)	0.090	**26.8**
Suitable for work	5.72 (0.20)	4.21 (0.21)	**35.08 (1.86)**	**<0.001**	0.01 (1.3)	0.908	0.10 (1.83)	0.758	**20.4**

EMM, estimated marginal means. SE, standard error. Pleasantness is a scale comprising four single items (pleasant, comfortable, disturbing and glary). All measures were derived from a 7-point semantic differential questionnaire completed at the beginning of the first night shift (time 1) and at the end of the last night shift (time 2). Estimates and statistics were calculated using linear mixed models. Adding the factors "time" and "light × time" interaction did not improve the model fit (Likelihood Ratio Test) for any of the variables. Significant findings are indicated in bold.

pleasant than 7000 K light, while 7000 K was evaluated as clearer, colder, brighter, more activating and more suitable for work than 2500 K light. Adding *light* as a factor significantly improved the model fit (*LRT*) compared with the random effects model for all measures (see explained variance in **Table 5**). For pleasantness, a significant interaction of *light* × *time* indicated that participants evaluated the 2500 K light as more pleasant than the 7000 K light only at time 2 (at the end of the third night shift).

However, the *LRT* indicated that the time-interaction model did not significantly improve the model fit for any of the variables compared with the main effects model.

DISCUSSION

In the current trial we applied novel strategies for administration of workplace lighting during three consecutive simulated night shifts, comparing blue-enriched (7000 K) and warm (2500 K) white light with similar photon density ($\sim 1.6 \times 10^{14}$ photons/cm^2/s). As expected, subjective and behavioral alertness deteriorated throughout the night shifts. Blue-enriched light was more beneficial for alertness during night shifts compared to 2500 K light, but the differences were not clear-cut and mainly manifested as fewer PVT performance errors (lapses and false starts) at the end of the first and second night shift. Overall, subjective alertness was higher with 7000 K, compared to 2500 K light, but there were no significant interaction effects of light and time. Similarly, for the DSST there were more correct responses with 7000 K light, but no significant interaction of light and time. For the PVT mean 1/RT there were indications of shorter RTs with 7000 K light in the mid–late parts of the night shifts, albeit not statistically significant. However, for the fastest 10% RT, there were significantly shorter RTs with 7000 K light at 02:30 and 04:00 h, compared to 2500 K light. Altogether, our hypothesis that 7000 K compared to 2500 K light would increase alertness and performance during night shifts received partly support. For those with valid phase shift estimates ($n = 20$ (69.0%) and $n = 22$ (78.6%) in 7000 and 2500 K light, respectively], the melatonin rhythm was phase delayed after the night shifts. However, there was no significant difference in terms of circadian phase shifts between the two light conditions. Due to missing data the latter finding is inconclusive.

Monochromatic short-wavelength (i.e., blue) light has been shown to elicit alerting responses (Cajochen et al., 2005; Lockley et al., 2006). Although responses to polychromatic light may differ from responses to monochromatic light (Revell et al., 2010; Figueiro et al., 2018), polychromatic blue-enriched (6500 K; 40 lx) light has also been found to induce alertness compared to warm (2500 K; 40 lx) light in the evening (Chellappa et al., 2011). Likewise, we found evidence of alerting responses to blue-enriched light during simulated night work.

In a recent study, LED-based room lighting (∼150 lx) with high (4667 K), moderate (3366 K), and low (2166 K) color temperature during simulated night work, however, did not differentially impact perceived alertness and performance on a 25 min visual PVT (Canazei et al., 2017). The relatively lower color temperature employed in that study may explain the lack of differences between light conditions compared to the present study. Additionally, the PVT's comparability with the version used in the present study is limited, as there were considerably fewer stimuli and substantially longer interstimulus intervals in the PVT applied by Canazei et al. (2017). Two other recent studies, using fluorescent light sources, assessed effects of nocturnal blue-enriched light on alertness and performance among real night workers (Motamedzadeh et al., 2017; Sletten et al., 2017). Similar to our findings concerning sleepiness, Sletten et al. (2017) found no differences between night workers exposed to blue-enriched light (17000 K; 89 lx) compared to standard light (4000 K; 84 lx). In addition, no differences regarding PVT performance was reported (Sletten et al., 2017). Sletten et al. (2017) did not use a crossover design, and between-subject differences may have confounded comparisons across conditions. The study by Sletten et al. (2017) also differed from the present study, as the light intervention commenced during one simulated night shift, following at least two consecutive night shifts at the participants' usual occupation. Enhanced alertness with blue-enriched light was reported by Motamedzadeh et al. (2017), with lower subjective sleepiness among control room operators during 12 h night shifts with medium (6500 K) and high (17,000 K) blue-enriched light (∼350 lx), compared to standard light (4000 K; ∼350 lx). On a Continuous Performance Test, blue-enriched light did not affect errors of commission, but 6500 and 17,000 K light favored attention in terms of shorter RTs, and for 17,000 K light there were also fewer errors of omission (Motamedzadeh et al., 2017). Similarly, the present study found fewer PVT lapses (i.e., errors of omission) in the later parts of the first and second shift with 7000 K light, but also fewer PVT false starts (i.e., errors of commission). In addition, there were indications of shorter RTs with 7000 K light, as performance in the optimal (i.e., fastest 10% RT) domain of the PVT was improved with 7000 K light compared to 2500 K light. While slow PVT RTs (i.e., lapses) have been associated with activation of brain regions involved in the default mode network (i.e., resting state), performance in the optimal domain of the PVT has been associated with activation of regions involved in the fronto-parietal sustained attention network (Drummond et al., 2005), suggesting modulation by the nonvisual system via the blue light sensitive ipRGCs (Vandewalle et al., 2009; Chellappa et al., 2011; Warthen and Provencio, 2012). Contrary to the findings by Chellappa et al. (2011), we also found beneficial effects of blue-enriched light regarding PVT lapses, hence the nonvisual system may also modulate the default mode network related to slow RTs and lapses (Drummond et al., 2005).

None of the previous studies investigating blue-enriched light assessed performance using DSST. However, in a recent study we found that performance on the DSST during simulated night work may be improved by nocturnal bright (4000 K; ∼900 lx) compared to standard (4000 K; ∼90 lx) light (Sunde et al., 2020). The DSST is sensitive to change in cognitive function, and both attention and working memory are required for optimal performance (Jaeger, 2018). In the study by Motamedzadeh et al. (2017), a working memory test (n-back) revealed more correct responses with 17,000 K compared to 4000 K light, although Canazei et al. (2017) found no differences between light conditions on a working memory task.

Compared to the present study, the color temperature (17,000 K) was higher in the study by Sletten et al. (2017), yet the illuminance (89 lx) was substantially lower. Overall, the melanopic illuminance of the 7000 K light (192 lx) in the present study was higher than in the 17,000 K (129 lx) light in Sletten et al. (2017). However, the relative difference between the compared light conditions within the present study and

the study by Sletten et al. (2017) was similar, with the blue-enriched light having about twice the melanopic illuminance as the control condition. Sletten et al. (2017) suggested that lack of differences between light conditions may reflect saturating light levels. Likewise, a highly controlled laboratory based study reported no differences in sleepiness between 9000 and 2800 K light (250 lx) and suggested that saturating light levels were used, and that spectral distribution is more important at lower light levels < 200 lx (Cajochen et al., 2019). Since in the present study higher illuminance was used than in Sletten et al. (2017), it cannot be ruled out that light saturation also influenced the current results. Still, in the study by Motamedzadeh et al. (2017), beneficial effects of blue-enriched light were found although the illuminance (∼350 lx) was even higher than in the present study.

It should be noted that previous studies concerning polychromatic light with different spectral distribution during night work (Canazei et al., 2017; Motamedzadeh et al., 2017; Sletten et al., 2017) have mainly used similar illuminance levels between the light conditions rather than being photon-matched. In the present study, however, the light conditions had similar photon density (∼1.6×10^{14}), thus being the first blue-enriched light during night work study that has directly assessed the effectiveness of short-wavelength compared to long-wavelength light whilst correctly controlling for light intensity/photon density. Photon-matching was also used in a recent and highly controlled (e.g., participants were studied in a time-free environment for 7 days) laboratory trial (Hanifin et al., 2019), assessing alerting effects of nocturnal 6.5 h exposure to blue-enriched (17,000 K; 96 lx; 1.00×10^{14} photons/cm^2/s) compared to standard (4000 K; 123 lx; 1.01×10^{14} photons/cm^2/s) light. Subjective sleepiness was reduced with 17,000 K light compared to standard light, but 17,000 K light did not affect PVT measured RTs or lapses during light exposure (Hanifin et al., 2019). Hanifin et al. (2019) applied lower illuminance and a different spectral distribution compared to the present study. However, in the study by Hanifin et al. (2019) the melanopic illuminance in the standard (79 lx) light was only slightly lower than in the 2500 K (86 lx) light used in the present study, while the 17,000 K (133 lx) light in Hanifin et al. (2019) had lower melanopic illumination than the 7000 K (192 lx) light in the present study. Thus, it is a little surprising that we did not find stronger effects of 7000 K light on subjective alertness/sleepiness, as the mechanism is thought to be mediated by melanopsin expressing ipRGCs projecting to brain areas important for alertness and arousal regulation (Vandewalle et al., 2009; Warthen and Provencio, 2012). Still, compared to our study, much more rigorous control of participants' exposure was taken, e.g., an ophthalmologic head holder was used to maintain a fixed head position and gaze, and light history was controlled with dim light and blindfolds prior to light exposure (Hanifin et al., 2019). As we found beneficial effects of 7000 K compared to 2500 K light on PVT measures, it is somewhat surprising that no effects were found during blue-enriched light exposure in the more controlled study by Hanifin et al. (2019).

In terms of polychromatic blue-enriched light, recent studies have not found greater phase delay with blue-enriched (17,000 K) compared to photon-matched standard (∼4000 K) light (Smith and Eastman, 2009; Hanifin et al., 2019), similar to the results in the present study. In the study by Smith and Eastman (2009), the blue-enriched light had a much higher illuminance (∼4000 lx) than in the current study and is thus not directly comparable. In the study by Hanifin et al. (2019), the light levels (1×10^{14} photons/cm^2/s) were lower and more comparable to the current study. Although the current results are in line with the findings by Hanifin et al. (2019), the study protocols differ substantially. Importantly, in the current study the light exposure was kept constant throughout the night shifts, hence a portion of light exposure occurred after the estimated Tmin for most participants. In line with the phase response curve to light (Khalsa et al., 2003; Revell et al., 2012), and the fact that 7000 K light had about twice the melanopic illuminance than 2500 K light, it is likely that 7000 K light exposure after Tmin attenuated the phase delay to a larger degree than 2500 K light. Despite the fact that there were no significant differences in the phase delay magnitude between 7000 and 2500 K light, we observed beneficial effects of 7000 K light for PVT performance measures. Thus, blue-enriched light, as administered in the present study, may improve behavioral alertness without inducing larger phase delay than warmer light. This can be regarded as beneficial because circadian adaption to night work, implies that one later would also need to readapt to a day work schedule. Hence, for short-term night work (no more than 3 nights) it is not desirable to fully adapt during the night work period.

Participants evaluated 7000 K light as colder, brighter and more activating than 2500 K light, similar to a previous study of fluorescent light (6000 K vs. 2700 K light) during daytime office hours (Smolders and de Kort, 2017). Participants' evaluation of 7000 K light as more activating than 2500 K light, contrasts the findings for the sleepiness and performance measures, where only minor advantages were found for 7000 K light. Thus, there may be some mismatch between subjective impressions of light effects and the actual test data on alertness and performance. In line with Smolders and de Kort (2017), participants evaluated 2500 K as more pleasant than 7000 K light. In contrast to lack of perceived differences during daytime office hours (Smolders and de Kort, 2017), 7000 K light was evaluated as clearer and more suitable for night work than 2500 K light. Thus, visual perception and appraisal of light conditions may differ during daytime and nighttime, possibly due to circadian and/or homeostatic processes also affecting subjective preferences for lighting. Noticeably, although there were differences in the evaluation of the pleasantness of the lights and their suitability for work, the participants evaluated both 7000 and 2500 K light as fairly pleasant and suitable for work.

Some limitations of the present study should be noted. Caution should be taken when interpreting the circadian phase shifting responses in the present study, as several participants (6 with 7000 K light and 3 with 2500 K light) did not reach the 3 pg/mL threshold during DLMO sampling after the night shifts, possibly because the light may have phase delayed DLMO beyond the fixed sampling time. Hence, it is possible that the 7000 K light caused a larger phase delay than could be measured, and the findings should be considered inconclusive. As for alertness and performance, saturating light levels may

also explain lack of significant phase shift differences. In terms of external validity, several factors need to be considered when interpreting the present results. Most participants were females and given that male participants have shown greater responses to blue-enriched light (Chellappa et al., 2017), the results may not be generalizable to populations with a different sex distribution. Although menstrual phase is known to impact PVT performance (Vidafar et al., 2018), only three female participants were estimated to be in a different menstrual phase during the two study periods. However, as these were rough estimates based on self-report, we cannot completely rule out that menstrual phase may have affected the results. None of the participants had color vision deficiency according to the Ishihara test, but some females can be tetrachromatic, i.e., express a fourth cone pigment (Jacobs, 2018), and we do not know if such alterations occurred or may have affected the results. The crossover and counterbalanced design, however, reduced this impact. We only studied young healthy participants and, as age differences in the responses to blue-enriched polychromatic light have been reported (Gabel et al., 2017), the transferability to real-life settings including older workers is not clear. Another point is that the present study was conducted at a latitude and at a time of year where daylight exposure was limited in the hours before and after the night shifts. Thus, the generalizability to other latitudes and/or other seasons can be questioned, as prior light exposure may affect the alerting responses to light (Chang et al., 2013). In addition, reduced exposure to morning light after night shifts (e.g., during the commute home) can hasten circadian adaptation to night work (Smith et al., 2008). We did not tailor an individually adapted light intervention which could be beneficial considering the large variability in individuals' circadian timing (Stone et al., 2018), and that individual differences in responses to light have been found (Phillips et al., 2019). However, in a real workplace, individually adapted light exposure using standard room lighting may be impractical, hence the current light intervention is generally more feasible and practical for workplaces. Still, it is now possible using modern LED technology to locally adjust the intensity and spectral distribution to facilitate desired nonvisual responses for individual workers. This should thus be explored in future studies. An issue regarding the use of LED-based blue-enriched light are potential hazards to the eyes, such as photochemical damage to the retina (Bullough et al., 2019), due to the blue-light exposure. However, reasonable foreseeable usage of LEDs is not expected to cause acute retinal damage, though possible long-term effects of exposure to new light sources need further research (International Commission on Non-Ionizing Radiation Protection, 2020).

In terms of study strengths we employed light conditions that are suitable for real-life application, and both conditions complied with European lighting standards for offices (CEN, 2011). Hence, compared to many previous studies of blue-enriched light (e.g., Chellappa et al., 2011; Hanifin et al., 2019), the current light conditions may be more suitable for a real-life workplace. We did not put requirements on participants' behavior during spare time away from the laboratory, e.g., in terms of activities, sleep timing and light exposure, as we wanted to employ a protocol that was transferable to a real work schedule as much as possible which may be viewed as an asset in terms of generalizability. The light sources were photon-matched thus the effect of spectral composition was not confounded by differences in light intensity. Furthermore, light conditions were administered using standard ceiling mounted LED-luminaires that can easily be installed at a real workplace. In addition, the crossover design adjusted for individual differences that otherwise could have exerted a strong effect on the outcome variables.

CONCLUSION

The present study indicated that standard LED-based polychromatic blue-enriched light (7000 K; ∼200 lx) compared to warm white light (2500 K) of similar photon density (∼1.6 × 10^{14} photons/cm^2/s), had significant and beneficial, albeit minor impact on the alertness and performance decrements experienced during simulated night work. The circadian phase was delayed with both light conditions with no significant differences between conditions. However, the circadian phase shift findings were inconclusive due to missing data. Participants' opinions of both light conditions were fairly positive, although 7000 K light was evaluated as more suitable for work, while 2500 K light was evaluated as more pleasant. In conclusion, LED-based blue-enriched light may facilitate alertness and performance during night work. More studies are needed to validate this conclusion, e.g., in different populations.

We encourage further research that makes full use of tunable LEDs, to elucidate lighting conditions favorable for night workers. Light interventions should be carefully planned to consider the various effects (e.g., subjective, cognitive and entrainment) of different light intensities and spectral distributions, and future studies in real workplaces are warranted to develop recommendations regarding illumination for night workers.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation, to any qualified researcher.

ETHICS STATEMENT

The study was reviewed and approved by the Regional Committee for Medical and Health Research Ethics, health region West, Norway (No. 2016/1903). The participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

SP assisted by BB, JG, AH, SW, and ES: conceptualization. ES, JM, TP, ET, JG, BB, AH, SW, and SP: study design. ES, JM, TP, and DS:

finalizing light conditions. ES, JM, TP, and ET: data collection. ES: data analysis. ES and SP: drafting the manuscript. ES, JM, TP, ET, JG, BB, AH, SW, DS, and SP: writing final draft. All authors contributed to the article and approved the submitted version.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Doctoral Theses at The Faculty of Psychology, University of Bergen

1980	Allen, Hugh M., Dr. philos.	Parent-offspring interactions in willow grouse (Lagopus L. Lagopus).
1981	Myhrer, Trond, Dr. philos.	Behavioral Studies after selective disruption of hippocampal inputs in albino rats.
1982	Svebak, Sven, Dr. philos.	The significance of motivation for task-induced tonic physiological changes.
1983	Myhre, Grete, Dr. philos.	The Biopsychology of behavior in captive Willow ptarmigan.
	Eide, Rolf, Dr. philos.	PSYCHOSOCIAL FACTORS AND INDICES OF HEALTH RISKS. The relationship of psychosocial conditions to subjective complaints, arterial blood pressure, serum cholesterol, serum triglycerides and urinary catecholamines in middle aged populations in Western Norway.
	Værnes, Ragnar J., Dr. philos.	Neuropsychological effects of diving.
1984	Kolstad, Arnulf, Dr. philos.	Til diskusjonen om sammenhengen mellom sosiale forhold og psykiske strukturer. En epidemiologisk undersøkelse blant barn og unge.
	Løberg, Tor, Dr. philos.	Neuropsychological assessment in alcohol dependence.
1985	Hellesnes, Tore, Dr. philos.	Læring og problemløsning. En studie av den perseptuelle analysens betydning for verbal læring.
	Håland, Wenche, Dr. philos.	Psykoterapi: relasjon, utviklingsprosess og effekt.
1986	Hagtvet, Knut A., Dr. philos.	The construct of test anxiety: Conceptual and methodological issues.
	Jellestad, Finn K., Dr. philos.	Effects of neuron specific amygdala lesions on fear-motivated behavior in rats.
1987	Aarø, Leif E., Dr. philos.	Health behaviour and sosioeconomic Status. A survey among the adult population in Norway.
	Underlid, Kjell, Dr. philos.	Arbeidsløyse i psykososialt perspektiv.
	Laberg, Jon C., Dr. philos.	Expectancy and classical conditioning in alcoholics' craving.
	Vollmer, Fred, Dr. philos.	Essays on explanation in psychology.
	Ellertsen, Bjørn, Dr. philos.	Migraine and tension headache: Psychophysiology, personality and therapy.
1988	Kaufmann, Astrid, Dr. philos.	Antisosial atferd hos ungdom. En studie av psykologiske determinanter.

	Mykletun, Reidar J., Dr. philos.	Teacher stress: personality, work-load and health.
	Havik, Odd E., Dr. philos.	After the myocardial infarction: A medical and psychological study with special emphasis on perceived illness.
1989	Bråten, Stein, Dr. philos.	Menneskedyaden. En teoretisk tese om sinnets dialogiske natur med informasjons- og utviklingspsykologiske implikasjoner sammenholdt med utvalgte spedbarnsstudier.
	Wold, Bente, Dr. psychol.	Lifestyles and physical activity. A theoretical and empirical analysis of socialization among children and adolescents.
1990	Flaten, Magne A., Dr. psychol.	The role of habituation and learning in reflex modification.
1991	Alsaker, Françoise D., Dr. philos.	Global negative self-evaluations in early adolescence.
	Kraft, Pål, Dr. philos.	AIDS prevention in Norway. Empirical studies on diffusion of knowledge, public opinion, and sexual behaviour.
	Endresen, Inger M., Dr. philos.	Psychoimmuniological stress markers in working life.
	Faleide, Asbjørn O., Dr. philos.	Asthma and allergy in childhood. Psychosocial and psychotherapeutic problems.
1992	Dalen, Knut, Dr. philos.	Hemispheric asymmetry and the Dual-Task Paradigm: An experimental approach.
	Bø, Inge B., Dr. philos.	Ungdoms sosiale økologi. En undersøkelse av 14-16 åringers sosiale nettverk.
	Nivison, Mary E., Dr. philos.	The relationship between noise as an experimental and environmental stressor, physiological changes and psychological factors.
	Torgersen, Anne M., Dr. philos.	Genetic and environmental influence on temperamental behaviour. A longitudinal study of twins from infancy to adolescence.
1993	Larsen, Svein, Dr. philos.	Cultural background and problem drinking.
	Nordhus, Inger Hilde, Dr. philos.	Family caregiving. A community psychological study with special emphasis on clinical interventions.
	Thuen, Frode, Dr. psychol.	Accident-related behaviour among children and young adolescents: Prediction and prevention.
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	Johnsen, Bjørn Helge, Dr. psychol.	Brain assymetry and facial emotional expressions: Conditioning experiments.
1994	Tønnessen, Finn E., Dr. philos.	The etiology of Dyslexia.
	Kvale, Gerd, Dr. psychol.	Psychological factors in anticipatory nausea and vomiting in cancer chemotherapy.

	Asbjørnsen, Arve E., Dr. psychol.	Structural and dynamic factors in dichotic listening: An interactional model.
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	Johannessen, Birte F., Dr. philos.	Det flytende kjønnet. Om lederskap, politikk og identitet.
1995	Sam, David L., Dr. psychol.	Acculturation of young immigrants in Norway: A psychological and socio-cultural adaptation.
	Bjaalid, Inger-Kristin, Dr. philos.	Component processes in word recognition.
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	Brun, Wibecke, Dr. philos.	Subjective conceptions of uncertainty and risk.
	Aas, Henrik N., Dr. psychol.	Alcohol expectancies and socialization: Adolescents learning to drink.
	Bjørkly, Stål, Dr. psychol.	Diagnosis and prediction of intra-institutional aggressive behaviour in psychotic patients
1996	Anderssen, Norman, Dr. psychol.	Physical activity of young people in a health perspective: Stability, change and social influences.
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	Øygard, Lisbet, Dr. philos.	Health behaviors among young adults. A psychological and sociological approach
	Stormark, Kjell Morten, Dr. psychol.	Emotional modulation of selective attention: Experimental and clinical evidence.

	Einarsen, Ståle, Dr. psychol.	Bullying and harassment at work: epidemiological and psychosocial aspects.
1997	Knivsberg, Ann-Mari, Dr. philos.	Behavioural abnormalities and childhood psychopathology: Urinary peptide patterns as a potential tool in diagnosis and remediation.
	Eide, Arne H., Dr. philos.	Adolescent drug use in Zimbabwe. Cultural orientation in a global-local perspective and use of psychoactive substances among secondary school students.
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	Jakobsen, Reidar, Dr. psychol.	Empiriske studier av kunnskap og holdninger om hiv/aids og den normative seksuelle utvikling i ungdomsårene.
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	Binder, Per-Einar, Dr. psychol.	Individet og den meningsbærende andre. En teoretisk undersøkelse av de mellommenneskelige forutsetningene for psykisk liv og utvikling med utgangspunkt i Donald Winnicotts teori.
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	Rosén, Gunnar O. R., Dr. philos.	The phantom limb experience. Models for understanding and treatment of pain with hypnosis.
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	Dyregrov, Kari, Dr. philos.	The loss of child by suicide, SIDS, and accidents: Consequences, needs and provisions of help.
2004 V	Torsheim, Torbjørn, Dr. psychol.	Student role strain and subjective health complaints: Individual, contextual, and longitudinal perspectives.

	Haugland, Bente Storm Mowatt Dr. psychol.	Parental alcohol abuse. Family functioning and child adjustment.
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	Mæhle, Magne, Dr. philos.	Re-inventing the child in family therapy: An investigation of the relevance and applicability of theory and research in child development for family therapy involving children.
	Kobbeltvedt, Therese, Dr. psychol.	Risk and feelings: A field approach.
2004 H	Thomsen, Tormod, Dr. psychol.	Localization of attention in the brain.
	Løberg, Else-Marie, Dr. psychol.	Functional laterality and attention modulation in schizophrenia: Effects of clinical variables.
	Kyrkjebø, Jane Mikkelsen, Dr. philos.	Learning to improve: Integrating continuous quality improvement learning into nursing education.
	Laumann, Karin, Dr. psychol.	Restorative and stress-reducing effects of natural environments: Experiencal, behavioural and cardiovascular indices.
	Holgersen, Helge, PhD	Mellom oss - Essay i relasjonell psykoanalyse.
2005 V	Hetland, Hilde, Dr. psychol.	Leading to the extraordinary? Antecedents and outcomes of transformational leadership.
	Iversen, Anette Christine, Dr. philos.	Social differences in health behaviour: the motivational role of perceived control and coping.
2005 H	Mathisen, Gro Ellen, PhD	Climates for creativity and innovation: Definitions, measurement, predictors and consequences.
	Sævi, Tone, Dr. philos.	Seeing disability pedagogically – The lived experience of disability in the pedagogical encounter.
	Wiium, Nora, PhD	Intrapersonal factors, family and school norms: combined and interactive influence on adolescent smoking behaviour.
	Kanagaratnam, Pushpa, PhD	Subjective and objective correlates of Posttraumatic Stress in immigrants/refugees exposed to political violence.
	Larsen, Torill M. B. , PhD	Evaluating principals` and teachers` implementation of Second Step. A case study of four Norwegian primary schools.
	Bancila, Delia, PhD	Psychosocial stress and distress among Romanian adolescents and adults.
2006 V	Hillestad, Torgeir Martin, Dr. philos.	Normalitet og avvik. Forutsetninger for et objektivt psykopatologisk avviksbegrep. En psykologisk, sosial, erkjennelsesteoretisk og teorihistorisk framstilling.

	Nordanger, Dag Øystein, Dr. psychol.	Psychosocial discourses and responses to political violence in post-war Tigray, Ethiopia.
	Rimol, Lars Morten, PhD	Behavioral and fMRI studies of auditory laterality and speech sound processing.
	Krumsvik, Rune Johan, Dr. philos.	ICT in the school. ICT-initiated school development in lower secondary school.
	Norman, Elisabeth, Dr. psychol.	Gut feelings and unconscious thought: An exploration of fringe consiousness in implicit cognition.
	Israel, K Pravin, Dr. psychol.	Parent involvement in the mental health care of children and adolescents. Emperical studies from clinical care setting.
	Glasø, Lars, PhD	Affects and emotional regulation in leader-subordinate relationships.
	Knutsen, Ketil, Dr. philos.	HISTORIER UNGDOM LEVER – En studie av hvordan ungdommer bruker historie for å gjøre livet meningsfullt.
	Matthiesen, Stig Berge, PhD	Bullying at work. Antecedents and outcomes.
2006 H	Gramstad, Arne, PhD	Neuropsychological assessment of cognitive and emotional functioning in patients with epilepsy.
	Bendixen, Mons, PhD	Antisocial behaviour in early adolescence: Methodological and substantive issues.
	Mrumbi, Khalifa Maulid, PhD	Parental illness and loss to HIV/AIDS as experienced by AIDS orphans aged between 12-17 years from Temeke District, Dar es Salaam, Tanzania: A study of the children's psychosocial health and coping responses.
	Hetland, Jørn, Dr. psychol.	The nature of subjective health complaints in adolescence: Dimensionality, stability, and psychosocial predictors
	Kakoko, Deodatus Conatus Vitalis, PhD	Voluntary HIV counselling and testing service uptake among primary school teachers in Mwanza, Tanzania: assessment of socio-demographic, psychosocial and socio-cognitive aspects
	Mykletun, Arnstein, Dr. psychol.	Mortality and work-related disability as long-term consequences of anxiety and depression: Historical cohort designs based on the HUNT-2 study
	Sivertsen, Børge, PhD	Insomnia in older adults. Consequences, assessment and treatment.
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	Janvin, Carmen Ani Cristea, PhD	Cognitive impairment in patients with Parkinson's disease: profiles and implications for prognosis
	Braarud, Hanne Cecilie, Dr.psychol.	Infant regulation of distress: A longitudinal study of transactions between mothers and infants
	Tveito, Torill Helene, PhD	Sick Leave and Subjective Health Complaints

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	Thuen, Elin Marie, Dr.philos.	Learning environment, students' coping styles and emotional and behavioural problems. A study of Norwegian secondary school students.
	Solberg, Ole Asbjørn, PhD	Peacekeeping warriors – A longitudinal study of Norwegian peacekeepers in Kosovo
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	Svensen, Erling, PhD	WORK & HEALTH. Cognitive Activation Theory of Stress applied in an organisational setting.
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	Eichele, Tom, PhD	Electrophysiological and Hemodynamic Correlates of Expectancy in Target Processing
	Børhaug, Kjetil, Dr.philos.	Oppseding til demokrati. Ein studie av politisk oppseding i norsk skule.
	Eikeland, Thorleif, Dr.philos.	Om å vokse opp på barnehjem og på sykehus. En undersøkelse av barnehjemsbarns opplevelser på barnehjem sammenholdt med sanatoriebarns beskrivelse av langvarige sykehusopphold – og et forsøk på forklaring.
	Wadel, Carl Cato, Dr.philos.	Medarbeidersamhandling og medarbeiderledelse i en lagbasert organisasjon
	Vinje, Hege Forbech, PhD	Thriving despite adversity: Job engagement and self-care among community nurses
	Noort, Maurits van den, PhD	Working memory capacity and foreign language acquisition
2008 V	Breivik, Kyrre, Dr.psychol.	The Adjustment of Children and Adolescents in Different Post-Divorce Family Structures. A Norwegian Study of Risks and Mechanisms.
	Johnsen, Grethe E., PhD	Memory impairment in patients with posttraumatic stress disorder
	Sætrevik, Bjørn, PhD	Cognitive Control in Auditory Processing
	Carvalhosa, Susana Fonseca, PhD	Prevention of bullying in schools: an ecological model
2008 H	Brønnick, Kolbjørn Selvåg	Attentional dysfunction in dementia associated with Parkinson's disease.
	Posserud, Maj-Britt Rocio	Epidemiology of autism spectrum disorders
	Haug, Ellen	Multilevel correlates of physical activity in the school setting
	Skjerve, Arvid	Assessing mild dementia – a study of brief cognitive tests.

	Kjønniksen, Lise	The association between adolescent experiences in physical activity and leisure time physical activity in adulthood: a ten year longitudinal study
	Gundersen, Hilde	The effects of alcohol and expectancy on brain function
	Omvik, Siri	Insomnia – a night and day problem
2009 V	Molde, Helge	Pathological gambling: prevalence, mechanisms and treatment outcome.
	Foss, Else	Den omsorgsfulle væremåte. En studie av voksnes væremåte i forhold til barn i barnehagen.
	Westrheim, Kariane	Education in a Political Context: A study of Konwledge Processes and Learning Sites in the PKK.
	Wehling, Eike	Cognitive and olfactory changes in aging
	Wangberg, Silje C.	Internet based interventions to support health behaviours: The role of self-efficacy.
	Nielsen, Morten B.	Methodological issues in research on workplace bullying. Operationalisations, measurements and samples.
	Sandu, Anca Larisa	MRI measures of brain volume and cortical complexity in clinical groups and during development.
	Guribye, Eugene	Refugees and mental health interventions
	Sørensen, Lin	Emotional problems in inattentive children – effects on cognitive control functions.
	Tjomsland, Hege E.	Health promotion with teachers. Evaluation of the Norwegian Network of Health Promoting Schools: Quantitative and qualitative analyses of predisposing, reinforcing and enabling conditions related to teacher participation and program sustainability.
	Helleve, Ingrid	Productive interactions in ICT supported communities of learners
2009 H	Skorpen, Aina Øye, Christine	Dagliglivet i en psykiatrisk institusjon: En analyse av miljøterapeutiske praksiser
	Andreassen, Cecilie Schou	WORKAHOLISM – Antecedents and Outcomes
	Stang, Ingun	Being in the same boat: An empowerment intervention in breast cancer self-help groups
	Sequeira, Sarah Dorothee Dos Santos	The effects of background noise on asymmetrical speech perception
	Kleiven, Jo, dr.philos.	The Lillehammer scales: Measuring common motives for vacation and leisure behavior
	Jónsdóttir, Guðrún	Dubito ergo sum? Ni jenter møter naturfaglig kunnskap.
	Hove, Oddbjørn	Mental health disorders in adults with intellectual disabilities - Methods of assessment and prevalence of mental health disorders and problem behaviour
	Wageningen, Heidi Karin van	The role of glutamate on brain function

	Bjørkvik, Jofrid	God nok? Selvaktelse og interpersonlig fungering hos pasienter innen psykisk helsevern: Forholdet til diagnoser, symptomer og behandlingsutbytte
	Andersson, Martin	A study of attention control in children and elderly using a forced-attention dichotic listening paradigm
	Almås, Aslaug Grov	Teachers in the Digital Network Society: Visions and Realities. A study of teachers' experiences with the use of ICT in teaching and learning.
	Ulvik, Marit	Lærerutdanning som danning? Tre stemmer i diskusjonen
2010 V	Skår, Randi	Læringsprosesser i sykepleieres profesjonsutøvelse. En studie av sykepleieres læringserfaringer.
	Roald, Knut	Kvalitetsvurdering som organisasjonslæring mellom skole og skoleeigar
	Lunde, Linn-Heidi	Chronic pain in older adults. Consequences, assessment and treatment.
	Danielsen, Anne Grete	Perceived psychosocial support, students' self-reported academic initiative and perceived life satisfaction
	Hysing, Mari	Mental health in children with chronic illness
	Olsen, Olav Kjellevold	Are good leaders moral leaders? The relationship between effective military operational leadership and morals
	Riese, Hanne	Friendship and learning. Entrepreneurship education through mini-enterprises.
	Holthe, Asle	Evaluating the implementation of the Norwegian guidelines for healthy school meals: A case study involving three secondary schools
H	Hauge, Lars Johan	Environmental antecedents of workplace bullying: A multi-design approach
	Bjørkelo, Brita	Whistleblowing at work: Antecedents and consequences
	Reme, Silje Endresen	Common Complaints – Common Cure? Psychiatric comorbidity and predictors of treatment outcome in low back pain and irritable bowel syndrome
	Helland, Wenche Andersen	Communication difficulties in children identified with psychiatric problems
	Beneventi, Harald	Neuronal correlates of working memory in dyslexia
	Thygesen, Elin	Subjective health and coping in care-dependent old persons living at home
	Aanes, Mette Marthinussen	Poor social relationships as a threat to belongingness needs. Interpersonal stress and subjective health complaints: Mediating and moderating factors.
	Anker, Morten Gustav	Client directed outcome informed couple therapy

	Bull, Torill	Combining employment and child care: The subjective well-being of single women in Scandinavia and in Southern Europe
	Viig, Nina Grieg	Tilrettelegging for læreres deltakelse i helsefremmende arbeid. En kvalitativ og kvantitativ analyse av sammenhengen mellom organisatoriske forhold og læreres deltakelse i utvikling og implementering av Europeisk Nettverk av Helsefremmende Skoler i Norge
	Wolff, Katharina	To know or not to know? Attitudes towards receiving genetic information among patients and the general public.
	Ogden, Terje, dr.philos.	Familiebasert behandling av alvorlige atferdsproblemer blant barn og ungdom. Evaluering og implementering av evidensbaserte behandlingsprogrammer i Norge.
	Solberg, Mona Elin	Self-reported bullying and victimisation at school: Prevalence, overlap and psychosocial adjustment.
2011 V	Bye, Hege Høivik	Self-presentation in job interviews. Individual and cultural differences in applicant self-presentation during job interviews and hiring managers' evaluation
	Notelaers, Guy	Workplace bullying. A risk control perspective.
	Moltu, Christian	Being a therapist in difficult therapeutic impasses. A hermeneutic phenomenological analysis of skilled psychotherapists' experiences, needs, and strategies in difficult therapies ending well.
	Myrseth, Helga	Pathological Gambling - Treatment and Personality Factors
	Schanche, Elisabeth	From self-criticism to self-compassion. An empirical investigation of hypothesized change prosesses in the Affect Phobia Treatment Model of short-term dynamic psychotherapy for patients with Cluster C personality disorders.
	Våpenstad, Eystein Victor, dr.philos.	Det tempererte nærvær. En teoretisk undersøkelse av psykoterapautens subjektivitet i psykoanalyse og psykoanalytisk psykoterapi.
	Haukebø, Kristin	Cognitive, behavioral and neural correlates of dental and intra-oral injection phobia. Results from one treatment and one fMRI study of randomized, controlled design.
	Harris, Anette	Adaptation and health in extreme and isolated environments. From 78°N to 75°S.
	Bjørknes, Ragnhild	Parent Management Training-Oregon Model: intervention effects on maternal practice and child behavior in ethnic minority families
	Mamen, Asgeir	Aspects of using physical training in patients with substance dependence and additional mental distress
	Espevik, Roar	Expert teams: Do shared mental models of team members make a difference
	Haara, Frode Olav	Unveiling teachers' reasons for choosing practical activities in mathematics teaching

2011 H	Hauge, Hans Abraham	How can employee empowerment be made conducive to both employee health and organisation performance? An empirical investigation of a tailor-made approach to organisation learning in a municipal public service organisation.
	Melkevik, Ole Rogstad	Screen-based sedentary behaviours: pastimes for the poor, inactive and overweight? A cross-national survey of children and adolescents in 39 countries.
	Vøllestad, Jon	Mindfulness-based treatment for anxiety disorders. A quantitative review of the evidence, results from a randomized controlled trial, and a qualitative exploration of patient experiences.
	Tolo, Astrid	Hvordan blir lærerkompetanse konstruert? En kvalitativ studie av PPU-studenters kunnskapsutvikling.
	Saus, Evelyn-Rose	Training effectiveness: Situation awareness training in simulators
	Nordgreen, Tine	Internet-based self-help for social anxiety disorder and panic disorder. Factors associated with effect and use of self-help.
	Munkvold, Linda Helen	Oppositional Defiant Disorder: Informant discrepancies, gender differences, co-occuring mental health problems and neurocognitive function.
	Christiansen, Øivin	Når barn plasseres utenfor hjemmet: beslutninger, forløp og relasjoner. Under barnevernets (ved)tak.
	Brunborg, Geir Scott	Conditionability and Reinforcement Sensitivity in Gambling Behaviour
	Hystad, Sigurd William	Measuring Psychological Resiliency: Validation of an Adapted Norwegian Hardiness Scale
2012 V	Roness, Dag	Hvorfor bli lærer? Motivasjon for utdanning og utøving.
	Fjermestad, Krister Westlye	The therapeutic alliance in cognitive behavioural therapy for youth anxiety disorders
	Jenssen, Eirik Sørnes	Tilpasset opplæring i norsk skole: politikeres, skolelederes og læreres handlingsvalg
	Saksvik-Lehouillier, Ingvild	Shift work tolerance and adaptation to shift work among offshore workers and nurses
	Johansen, Venke Frederike	Når det intime blir offentlig. Om kvinners åpenhet om brystkreft og om markedsføring av brystkreftsaken.
	Herheim, Rune	Pupils collaborating in pairs at a computer in mathematics learning: investigating verbal communication patterns and qualities
	Vie, Tina Løkke	Cognitive appraisal, emotions and subjective health complaints among victims of workplace bullying: A stress-theoretical approach
	Jones, Lise Øen	Effects of reading skills, spelling skills and accompanying efficacy beliefs on participation in education. A study in Norwegian prisons.

2012 H	Danielsen, Yngvild Sørebø	Childhood obesity – characteristics and treatment. Psychological perspectives.
	Horverak, Jøri Gytre	Sense or sensibility in hiring processes. Interviewee and interviewer characteristics as antecedents of immigrant applicants' employment probabilities. An experimental approach.
	Jøsendal, Ola	Development and evaluation of BE smokeFREE, a school-based smoking prevention program
	Osnes, Berge	Temporal and Posterior Frontal Involvement in Auditory Speech Perception
	Drageset, Sigrunn	Psychological distress, coping and social support in the diagnostic and preoperative phase of breast cancer
	Aasland, Merethe Schanke	Destructive leadership: Conceptualization, measurement, prevalence and outcomes
	Bakibinga, Pauline	The experience of job engagement and self-care among Ugandan nurses and midwives
	Skogen, Jens Christoffer	Foetal and early origins of old age health. Linkage between birth records and the old age cohort of the Hordaland Health Study (HUSK)
	Leversen, Ingrid	Adolescents' leisure activity participation and their life satisfaction: The role of demographic characteristics and psychological processes
	Hanss, Daniel	Explaining sustainable consumption: Findings from cross-sectional and intervention approaches
	Rød, Per Arne	Barn i klem mellom foreldrekonflikter og samfunnsmessig beskyttelse
2013 V	Mentzoni, Rune Aune	Structural Characteristics in Gambling
	Knudsen, Ann Kristin	Long-term sickness absence and disability pension award as consequences of common mental disorders. Epidemiological studies using a population-based health survey and official ill health benefit registries.
	Strand, Mari	Emotional information processing in recurrent MDD
	Veseth, Marius	Recovery in bipolar disorder. A reflexive-collaborative exploration of the lived experiences of healing and growth when battling a severe mental illness
	Mæland, Silje	Sick leave for patients with severe subjective health complaints. Challenges in general practice.
	Mjaaland, Thera	At the frontiers of change? Women and girls' pursuit of education in north-western Tigray, Ethiopia
	Odéen, Magnus	Coping at work. The role of knowledge and coping expectancies in health and sick leave.
	Hynninen, Kia Minna Johanna	Anxiety, depression and sleep disturbance in chronic obstructive pulmonary disease (COPD). Associations, prevalence and effect of psychological treatment.

	Flo, Elisabeth	Sleep and health in shift working nurses
	Aasen, Elin Margrethe	From paternalism to patient participation? The older patients undergoing hemodialysis, their next of kin and the nurses: a discursive perspective on perception of patient participation in dialysis units
	Ekornås, Belinda	Emotional and Behavioural Problems in Children: Self-perception, peer relationships, and motor abilities
	Corbin, J. Hope	North-South Partnerships for Health: Key Factors for Partnership Success from the Perspective of the KIWAKKUKI
	Birkeland, Marianne Skogbrott	Development of global self-esteem: The transition from adolescence to adulthood
2013 H	Gianella-Malca, Camila	Challenges in Implementing the Colombian Constitutional Court's Health-Care System Ruling of 2008
	Hovland, Anders	Panic disorder – Treatment outcomes and psychophysiological concomitants
	Mortensen, Øystein	The transition to parenthood – Couple relationships put to the test
	Årdal, Guro	Major Depressive Disorder – a Ten Year Follow-up Study. Inhibition, Information Processing and Health Related Quality of Life
	Johansen, Rino Bandlitz	The impact of military identity on performance in the Norwegian armed forces
	Bøe, Tormod	Socioeconomic Status and Mental Health in Children and Adolescents
2014 V	Nordmo, Ivar	Gjennom nåløyet – studenters læringserfaringer i psykologutdanningen
	Dovran, Anders	Childhood Trauma and Mental Health Problems in Adult Life
	Hegelstad, Wenche ten Velden	Early Detection and Intervention in Psychosis: A Long-Term Perspective
	Urheim, Ragnar	Forståelse av pasientaggresjon og forklaringer på nedgang i voldsrate ved Regional sikkerhetsavdeling, Sandviken sykehus
	Kinn, Liv Grethe	Round-Trips to Work. Qualitative studies of how persons with severe mental illness experience work integration.
	Rød, Anne Marie Kinn	Consequences of social defeat stress for behaviour and sleep. Short-term and long-term assessments in rats.
	Nygård, Merethe	Schizophrenia – Cognitive Function, Brain Abnormalities, and Cannabis Use
	Tjora, Tore	Smoking from adolescence through adulthood: the role of family, friends, depression and socioeconomic status. Predictors of smoking from age 13 to 30 in the "The Norwegian Longitudinal Health Behaviour Study" (NLHB)
	Vangsnes, Vigdis	The Dramaturgy and Didactics of Computer Gaming. A Study of a Medium in the Educational Context of Kindergartens.

	Nordahl, Kristin Berg	Early Father-Child Interaction in a Father-Friendly Context: Gender Differences, Child Outcomes, and Protective Factors related to Fathers' Parenting Behaviors with One-year-olds
2014 H	Sandvik, Asle Makoto	Psychopathy – the heterogenety of the construct
	Skotheim, Siv	Maternal emotional distress and early mother-infant interaction: Psychological, social and nutritional contributions
	Halleland, Helene Barone	Executive Functioning in adult Attention Deficit Hyperactivity Disorder (ADHD). From basic mechanisms to functional outcome.
	Halvorsen, Kirsti Vindal	Partnerskap i lærerutdanning, sett fra et økologisk perspektiv
	Solbue, Vibeke	Dialogen som visker ut kategorier. En studie av hvilke erfaringer innvandrerungdommer og norskfødte med innvandrerforeldre har med videregående skole. Hva forteller ungdommenes erfaringer om videregående skoles håndtering av etniske ulikheter?
	Kvalevaag, Anne Lise	Fathers' mental health and child development. The predictive value of fathers' psychological distress during pregnancy for the social, emotional and behavioural development of their children
	Sandal, Ann Karin	Ungdom og utdanningsval. Om elevar sine opplevingar av val og overgangsprosessar.
	Haug, Thomas	Predictors and moderators of treatment outcome from high- and low-intensity cognitive behavioral therapy for anxiety disorders. Association between patient and process factors, and the outcome from guided self-help, stepped care, and face-to-face cognitive behavioral therapy.
	Sjølie, Hege	Experiences of Members of a Crisis Resolution Home Treatment Team. Personal history, professional role and emotional support in a CRHT team.
	Falkenberg, Liv Eggset	Neuronal underpinnings of healthy and dysfunctional cognitive control
	Mrdalj, Jelena	The early life condition. Importance for sleep, circadian rhythmicity, behaviour and response to later life challenges
	Hesjedal, Elisabeth	Tverrprofesjonelt samarbeid mellom skule og barnevern: Kva kan støtte utsette barn og unge?
2015 V	Hauken, May Aasebø	«*The cancer treatment was only half the work!»* A Mixed-Method Study of Rehabilitation among Young Adult Cancer Survivors
	Ryland, Hilde Katrin	Social functioning and mental health in children: the influence of chronic illness and intellectual function
	Rønsen, Anne Kristin	Vurdering som profesjonskompetanse. Refleksjonsbasert utvikling av læreres kompetanse i formativ vurdering

	Hoff, Helge Andreas	Thinking about Symptoms of Psychopathy in Norway: Content Validation of the Comprehensive Assessment of Psychopathic Personality (CAPP) Model in a Norwegian Setting
	Schmid, Marit Therese	Executive Functioning in recurrent- and first episode Major Depressive Disorder. Longitudinal studies
	Sand, Liv	Body Image Distortion and Eating Disturbances in Children and Adolescents
	Matanda, Dennis Juma	Child physical growth and care practices in Kenya: Evidence from Demographic and Health Surveys
	Amugsi, Dickson Abanimi	Child care practices, resources for care, and nutritional outcomes in Ghana: Findings from Demographic and Health Surveys
	Jakobsen, Hilde	The good beating: Social norms supporting men's partner violence in Tanzania
	Sagoe, Dominic	Nonmedical anabolic-androgenic steroid use: Prevalence, attitudes, and social perception
	Eide, Helene Marie Kjærgård	Narrating the relationship between leadership and learning outcomes. A study of public narratives in the Norwegian educational sector.
2015 H	Wubs, Annegreet Gera	Intimate partner violence among adolescents in South Africa and Tanzania
	Hjelmervik, Helene Susanne	Sex and sex-hormonal effects on brain organization of fronto-parietal networks
	Dahl, Berit Misund	The meaning of professional identity in public health nursing
	Røykenes, Kari	Testangst hos sykepleierstudenter: «Alternativ behandling»
	Bless, Josef Johann	The smartphone as a research tool in psychology. Assessment of language lateralization and training of auditory attention.
	Løvvik, Camilla Margrethe Sigvaldsen	Common mental disorders and work participation – the role of return-to-work expectations
	Lehmann, Stine	Mental Disorders in Foster Children: A Study of Prevalence, Comorbidity, and Risk Factors
	Knapstad, Marit	Psychological factors in long-term sickness absence: the role of shame and social support. Epidemiological studies based on the Health Assets Project.
2016 V	Kvestad, Ingrid	Biological risks and neurodevelopment in young North Indian children
	Sælør, Knut Tore	Hinderløyper, halmstrå og hengende snører. En kvalitativ studie av håp innenfor psykisk helse- og rusfeltet.
	Mellingen, Sonja	Alkoholbruk, partilfredshet og samlivsstatus. Før, inn i, og etter svangerskapet – korrelater eller konsekvenser?
	Thun, Eirunn	Shift work: negative consequences and protective factors

	Hilt, Line Torbjørnsen	The borderlands of educational inclusion. Analyses of inclusion and exclusion processes for minority language students
	Havnen, Audun	Treatment of obsessive-compulsive disorder and the importance of assessing clinical effectiveness
	Slåtten, Hilde	Gay-related name-calling among young adolescents. Exploring the importance of the context.
	Ree, Eline	Staying at work. The role of expectancies and beliefs in health and workplace interventions.
	Morken, Frøydis	Reading and writing processing in dyslexia
2016 H	Løvoll, Helga Synnevåg	Inside the outdoor experience. On the distinction between pleasant and interesting feelings and their implication in the motivational process.
	Hjeltnes, Aslak	Facing social fears: An investigation of mindfulness-based stress reduction for young adults with social anxiety disorder
	Øyeflaten, Irene Larsen	Long-term sick leave and work rehabilitation. Prognostic factors for return to work.
	Henriksen, Roger Ekeberg	Social relationships, stress and infection risk in mother and child
	Johnsen, Iren	«Only a friend» - The bereavement process of young adults who have lost a friend to a traumatic death. A mixed methods study.
	Helle, Siri	Cannabis use in non-affective psychoses: Relationship to age at onset, cognitive functioning and social cognition
	Glambek, Mats	Workplace bullying and expulsion in working life. A representative study addressing prospective associations and explanatory conditions.
	Oanes, Camilla Jensen	Tilbakemelding i terapi. På hvilke måter opplever terapeuter at tilbakemeldingsprosedyrer kan virke inn på terapeutiske praksiser?
	Reknes, Iselin	Exposure to workplace bullying among nurses: Health outcomes and individual coping
	Chimhutu, Victor	Results-Based Financing (RBF) in the health sector of a low-income country. From agenda setting to implementation: The case of Tanzania
	Ness, Ingunn Johanne	The Room of Opportunity. Understanding how knowledge and ideas are constructed in multidisciplinary groups working with developing innovative ideas.
	Hollekim, Ragnhild	Contemporary discourses on children and parenting in Norway. An empirical study based on two cases.
	Doran, Rouven	Eco-friendly travelling: The relevance of perceived norms and social comparison
2017 V	Katisi, Masego	The power of context in health partnerships: Exploring synergy and antagony between external and internal ideologies in implementing Safe Male Circumcision (SMC) for HIV prevention in Botswana

	Jamaludin, Nor Lelawati Binti	The “why” and “how” of International Students’ Ambassadorship Roles in International Education
	Berthelsen, Mona	Effects of shift work and psychological and social work factors on mental distress. Studies of onshore/offshore workers and nurses in Norway.
	Krane, Vibeke	Lærer-elev-relasjoner, elevers psykiske helse og frafall i videregående skole – en eksplorerende studie om samarbeid og den store betydningen av de små ting
	Søvik, Margaret Ljosnes	Evaluating the implementation of the Empowering Coaching™ program in Norway
	Tonheim, Milfrid	A troublesome transition: Social reintegration of girl soldiers returning ‘home’
	Senneseth, Mette	Improving social network support for partners facing spousal cancer while caring for minors. A randomized controlled trial.
	Urke, Helga Bjørnøy	Child health and child care of very young children in Bolivia, Colombia and Peru.
	Bakhturidze, George	Public Participation in Tobacco Control Policy-making in Georgia
	Fismen, Anne-Siri	Adolescent eating habits. Trends and socio-economic status.
2017 H	Hagatun, Susanne	Internet-based cognitive-behavioural therapy for insomnia. A randomised controlled trial in Norway.
	Eichele, Heike	Electrophysiological Correlates of Performance Monitoring in Children with Tourette Syndrome. A developmental perspective.
	Risan, Ulf Patrick	Accommodating trauma in police interviews. An exploration of rapport in investigative interviews of traumatized victims.
	Sandhåland, Hilde	Safety on board offshore vessels: A study of shipboard factors and situation awareness
	Blågestad, Tone Fidje	Less pain – better sleep and mood? Interrelatedness of pain, sleep and mood in total hip arthroplasty patients
	Kronstad, Morten	Frå skulebenk til deadlines. Korleis nettjournalistar og journaliststudentar lærer, og korleis dei utviklar journalistfagleg kunnskap
	Vedaa, Øystein	Shift work: The importance of sufficient time for rest between shifts.
	Steine, Iris Mulders	Predictors of symptoms outcomes among adult survivors of sexual abuse: The role of abuse characteristics, cumulative childhood maltreatment, genetic variants, and perceived social support.
	Høgheim, Sigve	Making math interesting: An experimental study of interventions to encourage interest in mathematics

2018 V	Brevik, Erlend Joramo	Adult Attention Deficit Hyperactivity Disorder. Beyond the Core Symptoms of the Diagnostic and Statistical Manual of Mental Disorders.
	Erevik, Eilin Kristine	User-generated alcohol-related content on social media: Determinants and relation to offline alcohol use
	Hagen, Egon	Cognitive and psychological functioning in patients with substance use disorder; from initial assessment to one-year recovery
	Adólfsdóttir, Steinunn	Subcomponents of executive functions: Effects of age and brain maturations
	Brattabø, Ingfrid Vaksdal	Detection of child maltreatment, the role of dental health personnel – A national cross-sectional study among public dental health personnel in Norway
	Fylkesnes, Marte Knag	Frykt, forhandlinger og deltakelse. Ungdommer og foreldre med etnisk minoritetsbakgrunn i møte med den norske barnevernstjenesten.
	Stiegler, Jan Reidar	Processing emotions in emotion-focused therapy. Exploring the impact of the two-chair dialogue intervention.
	Egelandsdal, Kjetil	Clickers and Formative Feedback at University Lectures. Exploring students and teachers' reception and use of feedback from clicker interventions.
	Torjussen, Lars Petter Storm	Foreningen av visdom og veltalenhet – utkast til en universitetsdidaktikk gjennom en kritikk og videreføring av Skjervheims pedagogiske filosofi på bakgrunn av Arendt og Foucault. *Eller hvorfor menneskelivet er mer som å spille fløyte enn å bygge et hus.*
	Selvik, Sabreen	A childhood at refuges. Children with multiple relocations at refuges for abused women.
2018 H	Leino, Tony Mathias	Structural game characteristics, game features, financial outcomes and gambling behaviour
	Raknes, Solfrid	Anxious Adolescents: Prevalence, Correlates, and Preventive Cogntive Behavioural Interventions
	Morken, Katharina Teresa Enehaug	Mentalization-based treatment of female patients with severe personality disorder and substance use disorder
	Braatveit, Kirsten Johanne	Intellectual disability among in-patients with substance use disorders
	Barua, Padmaja	Unequal Interdependencies: Exploring Power and Agency in Domestic Work Relations in Contemporary India
	Darkwah, Ernest	Caring for "parentless" children. An exploration of work-related experiences of caregivers in children's homes in Ghana.
	Valdersnes, Kjersti Bergheim	Safety Climate perceptions in High Reliability Organizations – the role of Psychological Capital

2019 V	Kongsgården, Petter	Vurderingspraksiser i teknologirike læringsmiljøer. En undersøkelse av læreres vurderingspraksiser i teknologirike læringsmiljøer og implikasjoner på elevenes medvirkning i egen læringsprosess.
	Vikene, Kjetil	Complexity in Rhythm and Parkinson's disease: Cognitive and Neuronal Correlates
	Heradstveit, Ove	Alcohol- and drug use among adolescents. School-related problems, childhood mental health problems, and psychiatric diagnoses.
	Riise, Eili Nygard	Concentrated exposure and response prevention for obsessive-compulsive disorder in adolescents: the Bergen 4-day treatment
	Vik, Alexandra	Imaging the Aging Brain: From Morphometry to Functional Connectivity
	Krossbakken, Elfrid	Personal and Contextual Factors Influencing Gaming Behaviour. Risk Factors and Prevention of Video Game Addiction.
	Solholm, Roar	Foreldrenes status og rolle i familie- og nærmiljøbaserte intervensjoner for barn med atferdsvansker
	Baldomir, Andrea Margarita	Children at Risk and Mothering Networks in Buenos Aires, Argentina: Analyses of Socialization and Law-Abiding Practices in Public Early Childhood Intervention.
	Samuelsson, Martin Per	Education for Deliberative Democracy. Theoretical assumptions and classroom practices.
	Visted, Endre	Emotion regulation difficulties. The role in onset, maintenance and recurrence of major depressive disorder.
2019 H	Nordmo, Morten	Sleep and naval performance. The impact of personality and leadership.
	Sveinsdottir, Vigdis	Supported Employment and preventing Early Disability (SEED)
	Dwyer, Gerard Eric	New approaches to the use of magnetic resonance spectroscopy for investigating the pathophysiology of auditory-verbal hallucinations
	Synnevåg, Ellen Strøm	Planning for Public Health. Balancing top-down and bottom-up approaches in Norwegian municipalities.
	Kvinge, Øystein Røsseland	Presentation in teacher education. A study of student teachers' transformation and representation of subject content using semiotic technology.
	Thorsen, Anders Lillevik	The emotional brain in obsessive-compulsive disorder
	Eldal, Kari	Sikkerheitsnettet som tek imot om eg fell – men som også kan fange meg. Korleis erfarer menneske med psykiske lidingar ei innlegging i psykisk helsevern? Eit samarbeidsbasert forskingsprosjekt mellom forskarar og brukarar.

	Svendsen, Julie Lillebostad	Self-compassion - Relationship with mindfulness, emotional stress symptoms and psychophysiological flexibility
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